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# THE PRINCIPLES OF
# PHYSICS AND BIOLOGY
# OF
# RADIATION THERAPY

BY

**Dr. Bernhard Kroenig** and **Dr. Walter Friedrich**

Professor of Gynecology and Obstetrics, etc., University of Freiburg im Breisgau

Chief of Division of Radium Therapy, University of Freiburg im Breisgau

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ONLY AUTHORIZED ENGLISH EDITION
WITH AN APPENDIX

BY

DR. HENRY SCHMITZ

Professor of Gynecology and Head of Department, Loyola University School of Medicine, Chicago, Illinois

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WITH 86 TEXTUAL FIGURES AND 20 COLORED AND 11 BLACK AND WHITE PLATES, AND 32 TABLES

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## PREFACE

The translation of Krönig and Friedrich's book, "Die physikalischen und biologischen Grundlagen der Strahlentherapie," was made in response to innumerable requests of English-speaking physicians interested in radiation therapy. The monograph was the first to give a complete presentation of the scientific principles underlying this new branch of the specialties of medicine and surgery. By the correct application of these facts it is now possible to discard the empirical uncertainties of the therapeutic use of radiations and replace them by scientifically correct methods.

To bring the book to date the various investigations, carried on since its publication in 1918 in the Physical Institute at Freiburg by W. Friedrich and his associates and assistants, Otto Glasser, Hans Körner, M. Bender, Erich Huth and Henry Schmitz, have been added. Thereby the monograph has attained added value, as it gives information demonstrating the importance of Krönig and Friedrich's work on the progress of radiation therapy.

The translation was undertaken in a spirit partly of reluctance and partly of enthusiasm. Reluctantly because the task of translation is a difficult one if the translator endeavors to adhere closely and truthfully to the original text. Enthusiastically as by the publication of an English edition a tribute is paid to the untiring work of the late Prof. Krönig, whom we must regard as one of the fathers of radiation therapy. To his farsightedness is due the fact that the trained physicist has become associated with the clinician in the correct and scientific solution of the many problems of radiation therapy. The translation also serves as a tribute to the important work performed by Friedrich in association with Knipping in Prof. v. Laue's laboratory relative to the determination of the nature of the X-rays.

It is confidently expected that the book will be a worthy companion to the many important publications of similar investigations made by American physicists and physicians; that it will materially contribute to the development of radiation therapy in our country, and that thus suffering humanity may be immensely benefited by the newer therapy of radiation treatment.

Finally I express my appreciation to Dr. Gerald L. Wendt, Dr. Frank H. Doubler, and to my secretary, Miss Emma L. Harter, for their valuable assistance in correcting the manuscript.

I thank the publishers for their unselfish attitude in publishing the monograph.

HENRY SCHMITZ.

Chicago, Ill.

53065

## VORWORT ZUR AMERIKANISCHEN AUSGABE

Die Erkenntnis dass eine erfolgreiche Forschung auf dem Gebiete der Strahlentherapie nur möglich ist, wenn Biologe und Physiker zusammen arbeiten, hatte B. Krönig veranlasst mich nach Freiburg zu rufen. Die Früchte der gemeinsamen Arbeit der Jahre 1915-1916 haben wir in den "Physikalischen und biologischen Grundlagen" zusammengestellt. Die Gegenwart hat bewiesen, dass Krönig's Erkenntnis die richtige war. Die Fortschritte auf dem Gebiete der Strahlentherapie sind in den letzten Jahren ausserordentliche. Leider war es meinem hochverehrten Mitarbeiter nicht mehr möglich die Anerkennung seines Buches zu erleben. Er wurde vor dem Erscheinen des Buches durch eine tückische Krankheit dahingerafft.

Die Wissenschaft ist international. Der Weltkrieg hatte die Völker getrennt. Nur spärlich war ein Austausch der Forschungsarbeiten möglich. Jetzt nach Beendigung des Krieges ist die Möglichkeit gegeben, dass die Gelehrten der beiden Länder wiederum in wissenschaftlichen Kontakt kommen. Der Anfang ist gemacht. Schon 1920 konnten wir eine Anzahl amerikanischer Forscher in Freiburg begrüssen, die gekommen waren, um die alten wissenschaftlichen Beziehungen wieder anzuknüpfen. Auch hier gilt ja der Grundsatz, dass Zusammenarbeit die Forschung fördert. Ich begrüsste es daher ausserordentlich, als Herr Prof. Dr. H. Schmitz aus Chicago mir den Vorschlag machte unser Werk in die englische Sprache zu übersetzen, um es den amerikanischen Gelehrten zugänglicher zu machen. Die Persönlichkeit des Herrn Dr. Schmitz bietet mir vollauf Gewähr, dass die Übersetzung mustergültig sein wird.

In einem Anhange sind einige weitere Arbeiten angefügt aus dem gleichen Wissenszweig, die in der letzten Zeit im radiologischen Institut der Universität Freiburg gemacht sind, unter diesen eine, die Herr Dr. Schmitz in meinem Institute ausführen konnte über die Isodosen einiger in Amerika üblichen Bestrahlungsapparate der Radiumtherapie.

WALTER FRIEDRICH.

FREIBURG im Br.

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## PART I

# THE PHYSICAL PRINCIPLES OF RADIATION THERAPY

Roentgen and radium rays influence biologic processes in the vegetable and animal kingdom in many different ways. Medical science has attempted to make use of this action on biologic structures for purposes of treatment. It has on the one hand employed simple empirical experiments and on the other drawn conclusions for its purposes from experiments mostly carried on with living beings of a low order. The literature on this subject has become very voluminous, especially in recent years, yet one cannot state that really fixed laws and uniform results have been reported. The results of investigations made for experimental as well as therapeutic purposes differ greatly. The conclusions oftentimes are diametrically opposed to each other.

These great discrepancies may be explained in different ways. The researches may not have been carried on under like conditions. Two investigators may not have used the same methods of measurements in their experiments, so that the same quantities or qualities of radiations were not applied; or the biologic tests were made on too complicated objects, so that the results were different and were variously interpreted on account of the great number of uncontrollable factors.

We gained the impression in looking over the literature, that the differences in the results must be mainly looked for in the non-uniform methods of measuring and in the disregard of the sources of errors in the various methods of measuring. This increasing laxity in the measuring methods has been universally recognized and has found a visible expression in the appointment of a dosimeter commission at the last congress of roentgenologists. The labors of this commission have been delayed due to the war and have not as yet been definitely concluded. Therefore it was our first object to institute investigations on the methods of measuring, to determine the sources of error and to advise means to reduce them to a negligible minimum. Above all we had to decide on a method of measurement which could be uniformly employed in all biologic experimentation, for it must be recognized that only such biologic experiments may be compared in which the same methods of measuring are used.

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## ERRATA

| Page | Line | | |
|---|---|---|---|
| 40 | 3 | from top | *read* Gaede *instead of* Goede. |
| 52 | 8 | " bottom | *read* cm. square *instead of* sq. cm. |
| 60 | 3 | " top | *read* Szillard *instead of* Szilard. |
| 60 | 14 | " top | *read* Szillard *instead of* Szilard. |
| 60 | 27 | " top | *read* volume *instead of* volumes. |
| 62 | 12 | " bottom | *read* volume *instead of* capacity. |
| 64 | 12 | " top | *read* $C=\frac{(r+)^2}{16d}$ *instead of* $C=\frac{(r+r)2}{16d}$ |
| 67 | 10 | " top | *read* ventile *instead of* ventilation. |
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## PART I

# THE PHYSICAL PRINCIPLES OF RADIATION THERAPY

Roentgen and radium rays influence biologic processes in the vegetable and animal kingdom in many different ways. Medical science has attempted to make use of this action on biologic structures for purposes of treatment. It has on the one hand employed simple empirical experiments and on the other drawn conclusions for its purposes from experiments mostly carried on with living beings of a low order. The literature on this subject has become very voluminous, especially in recent years, yet one cannot state that really fixed laws and uniform results have been reported. The results of investigations made for experimental as well as therapeutic purposes differ greatly. The conclusions oftentimes are diametrically opposed to each other.

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ever, as it is much more frequently necessary to know the quantity of energy projected on the unit of surface within an arbitrary time limit and not the quantity of energy projected on the unit of surface within a unit of time, we adopt with Cristen *the definition of surface energy, which is the quantity of energy vertically projected on one square centimeter of surface.* It is expressed in the formula:

2) $$F = \frac{E}{f}$$

This quantity of energy may be produced either with a small intensity in a longer time or with a large intensity in a shorter time. Surface energy is therefore the product of intensity and time, and expressed in the following equation:

3) $$F = J \cdot t$$

Surface energy may always be traced back to the quotient of the radiation energy and the surface on which it is projected, or to the product of the intensity of the radiation multiplied with the time of application.

The formula must be corrected if the radiation is not perpendicularly projected on the unit of surface but at an oblique angle. We must add another factor, the cos. $\varphi$ of the angle formed by the normal of the surface with the axis of the radiation beam. It is not necessary to cite the geometrical discussion, as it has been described in extenso by Grossmann. Formula 3 is therefore changed to:

4) $$F = J \cdot t \cdot \cos. \varphi$$

and formula 2 to

5) $$F = \frac{E}{f} \cdot \cos. \varphi$$

## Definition of Hardness of Radiation

The process which leads to the formation of X-rays in a roentgen-tube is, according to our present views, as follows: The cathode rays emanating from the cathode are in their course focussed on the anticathode, or target, the surface of which is inclined at 45° to the rays. From the point of impact of the cathode rays on the anticathode X-rays are given out in all directions.

The view of the electro-magnetic wave character of the X-rays, which already had been accepted as probable from various properties of X-rays analogous to those of light-waves, found its final confirmation in the discovery of interference effects of X-rays when passing through crystals by one of us in association with M. v. Laue* and P. Knipping.

The wave-length of the electro-magnetic impulse depends on

* Münchener Berichte, 1912, p. 303.

the velocity with which the cathode rays hit the anticathode and on their penetration into the anticathode. The greater the velocity of the cathode rays and the less the depth to which they enter the anticathode the shorter is the wave-length of the impulse. The velocity of the electrons is dependent on the potential maintained between cathode and anode. The higher the voltage, the greater the velocity of the cathode-rays. The knowledge that the penetrability of the X-rays is dependent on the applied voltage, has shown that X-rays with short wave-lengths more easily penetrate media, i.e., they are harder than those with long wave-lengths. *The hardness of rays therefore is defined by the ability to penetrate.* As every impulse may be dissected into its component wave-lengths and as we are in a position through roentgen spectography to separate the different wave-lengths of the various impulses from each other, we could prove the dependence of penetrability on the wave-length. The investigations revealed the expected result that the degree of penetrability (hardness) is the greater, the shorter the wave-length.

The expression, which in physics characterizes the penetrability, is the *absorption-coefficient.* This is defined as the reciprocal thickness of a layer in which the intensity of the projected radiation is decreased to the e. part. The law which expresses it has the formula:

6) $$J_1 = J_o \,.\, e^{-\lambda d}$$

$J_o$ signifies the intensity of radiation projected onto the medium, $J_1$ the intensity remaining after passing through the medium, d the thickness of the penetrated layer, $\lambda$ the linear absorption-coefficient, while e is the basis of the hyperbolic system of logarithms. This simplest form of the law of absorption holds good only for rays *of the same wave-length,* i.e., *for homogeneous rays.* In reality, however, when dealing with X-rays we almost exclusively deal with rays of the most varied wave-lengths, i.e., heterogeneous or complex radiations. We, therefore, can only speak of *a mean absorption-coefficient.* The law (6) is the more complicated, the more radiation components are to be considered and is hardly amenable to numerical calculation.

Christen has introduced the conception of the *half absorption value layer,* as the conception of the absorption coefficient offers certain difficulties. He defines the half absorption value layer as the layer of a medium which absorbs one-half of the X-ray energy penetrating the same. The law of absorption according to Christen is thus expressed:

7) $$J_1 = J_o \left(\frac{1}{2}\right)^{\frac{d}{h}}$$

or expressed in words: If the penetrated layer d=h, then the intensity has been reduced by one-half to $\frac{1}{2}$ J. In the succeeding layer of the thickness h it is again reduced by one-half: $\frac{1}{2} \cdot \frac{1}{2} J = \frac{1}{4} J$. In the third layer to $\frac{1}{2} \cdot \frac{1}{4} J = \frac{1}{8} J$, etc.

To render more easy the conception of non-homogeneity or heterogeneity, Christen defines these as the quotient of the first two half absorption value layers. If, using a non-homogeneous radiation, we measure that the intensity of the radiation is decreased to one-half after passing through a layer of 2 cm., and the remaining intensity again is reduced by one-half in a second layer of 3 cm., then the heterogeneity is

$$H = \frac{3}{2}.$$

Quite analogous considerations hold good for the gamma-rays of radio-active substances, of which we shall use only radium and mesothorium in this study. The same definitions may be applied to these radiations.

## Definition of Dose

If we project the X-rays on any kind of an object a part of the rays will be absorbed in the body, another part will pass through it. If we observe any reactions, either of a chemical, a biologic, or a physical nature in the object, then all these reactions have been produced by the radiation energy absorbed in the medium. Medical science has agreed to designate the X-ray energy absorbed in a biologic object as the X-ray dose. If we term the energy projected on a biologic object $E_1$ and the energy remaining after passing through the medium $E_2$, then *the difference between the energies $E_1$—$E_2$ is the X-ray dose.*

The unit of the X-ray dose is the X-ray energy absorbed in a unit volume, i.e., in 1 ccm. of a biologic object. If the part of the biologic object exposed to the rays has the volume V, then the dose in this part is

8) $$D = \frac{E_1 - E_2}{V}$$

This dose is in reality only a mean dose, because the surface of the body traversed by the rays receives a larger dose than the deep layers, for the energy projected into the deeply located stratum is less on account of absorption in the layer above it. We therefore speak of a surface dose and a depth dose and define them as follows:

*Surface dose* means the X-ray energy absorbed in a very thin layer of the surface of the volume of 1 ccm.

*Depth dose* is the radiation energy absorbed in a very thin layer of the depth of the volume of 1 ccm.

Let us suppose a certain body of a certain thickness, the surface and base of which are parallel and level. Let the energy projected perpendicularly on 1 squ. cm. of the surface of the body during a certain time be the surface energy $F_o$ and $F_o = J : t$. J as customary, expresses the intensity.

Let the energy remaining at the base of this body during the same time per squ. cm. be the energy $F_1$ and $F_1 = J_1 \cdot t$.

The source of radiation is located so far distant from this body, that this distance of the source of radiation from the body is very great compared to the distance from surface to base. The decrease of the intensity from the surface to the base is then negligible according to the law of squares.

A radiation beam projected on 1 squ. cm. of the surface of this body will advance perpendicularly to the base and also project on 1 squ. cm. at the base. The body traversed by the radiation beam has the form of a rectangular prism, and the energy absorbed in the prismatic column of the body equals

$$\frac{F_o - F_1}{V} = D, \text{ the dose.}$$

V is the volume of the prismatic body.

If we further assume that the height of the prism, corresponding to the thickness of the body, equals the half absorption value layer h, then the intensity of the radiation at the base is equal to one-half the intensity of the radiation on the surface,

$$J_1 = \frac{1}{2} J.$$

and the dose is

$$D = \frac{\frac{1}{2} F_o}{V}$$

The volume V of the prismatic body is

$$1 \cdot h,$$

therefore

9) $$D = \frac{\frac{1}{2} F_o}{h}$$

Expressed in words it means: The dose is also defined by the surface energy and the half absorption value layer, and, indeed, the dose is directly proportional to the energy at that surface and indirectly proportional to the half absorption value layer. The half absorption value layer may be also replaced by the absorption coefficient.

# Measurement of Intensity, Hardness and Dose

## Measurement of Intensity of Rays

While the physicist in the measuring of the intensity of X-rays almost exclusively uses the ionization method or the method of the electric charge of a metallic body in turn exposed to X-rays, we find in medical literature the recommendation of various devices for measuring the intensity, such as the Sabouraud-Noiré tablets. Recently the instrument of Fürstenau

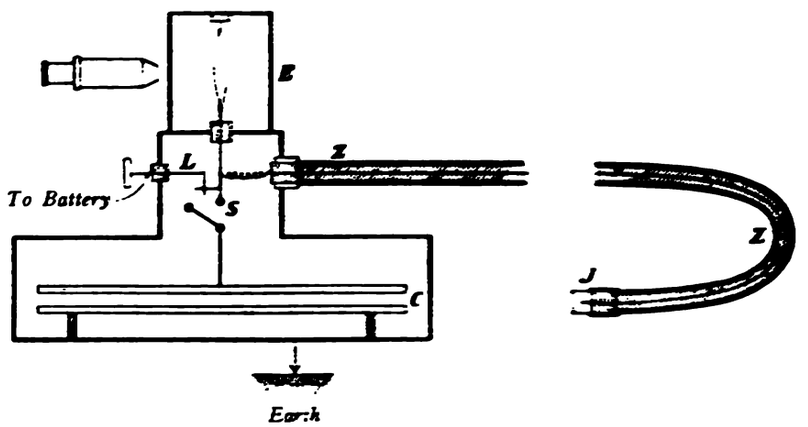


FIG. 1.

has been advocated. It is based on the change of resistance of selenium produced by the action of X-rays.

We have exclusively used the ionization method for measuring the intensity. The details of the experiments for carrying out such measurements of the intensity of X-rays and rays from radioactive substances are described in the following:

As it was necessary in the biologic experiments to be able to measure intensity at every point of the radiated medium, we gave the apparatus a form that permitted the introduction of the ionization chamber like a uterine dilator into the medium. The method of measuring consisted in the discharge of an electrometer charged with a known capacity. We used the Wulf two-leaf electrometer in which the degree of charge could be determined with a reading microscope from the more or less extensive deflection of the two charged quartz leaves. Fig. 1 gives a schematic picture of the

arrangement and Fig. 2 a photographic reproduction of the instrument.

The quartz fibers of the electrometer are connected with a wire to conductor Z, which consists of a very well rubber-insulated cable, which is surrounded by a grounded flexible metal protective layer. The other end of the cable extends into the ionization chamber J through a piece of amber which is shaped so that it fits exactly into the tube. For measuring the intensity we generally used a chamber of very thin aluminum leaf of a rectangular form, which had a volume of exactly 1 ccm. The rubber cable, which was of a length of about 2.50 m., has the advantage in comparison with the usually employed metal tubes filled with air, that an unde-

FIG. 2.

sired radiation carried in the conductor does not contribute to the discharge of the electrometer. The error of soaking up of the charge into the dielectric and the leakage of the electric residue of the electrometer during the discharge may be reduced to a negligible quantity, if one pays attention to the fact that the stationary stage of the dielectric polarization of the rubber has been attained and that the sensitiveness of the apparatus is so great that single measurements can be made within a very short time.

The electrometer could be connected through the switch S with a well-insulated plate condenser C to change its sensitiveness. The condenser reduced the latter by one-half. A charging arrangement L permitted loading the electrometer to the desired potential by turning a knob. A battery of cells of about 200 volts served for the production of the electric charge.

In the construction of the instrument special attention was paid that all the parts were well protected electrostatically, especially

that no part of the insulated cable entered the case of the electroscope during the process of measuring. This is considered an absolute necessity for accurate measurements on account of the high frequency oscillations in the X-ray room. The instrument also could be used for the measurement of the intensity of the gamma-rays derived from radio-active substances.

However, another method was employed when measuring the intensity of rays of radio-active substances, especially if the preparations were weak.

The high penetrability of gamma-rays and the great dangers connected therewith that a source of error might arise from this

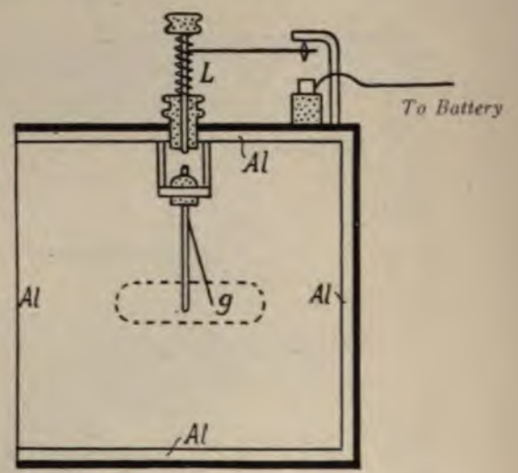


FIG. 3.

behavior, made it appear advantageous to let the electrometer also serve as ionization chamber. The only space within which the rays then cause a discharge of the electrometer by ionization is the instrument itself. The electrometer was composed of a rectangular lead box of a content of 1 liter; the walls were 5 mm. thick. See Figs. 3 and 4. Within this box was the gold leaf G which served for the measuring. It was suspended from a holder of aluminum, which was insulated with amber. The wall of the electrometer, exposed to the source of the radiation to be measured, was formed of an aluminum sheet of 0.03 mm. thickness (Al.). It could be replaced with thinner or heavier sheets of various substances corresponding to the different conditions under investigation. The inner surfaces of the instrument were lined with sheets of aluminum (Al.) 5 mm. thick. We considered it correct to take this precaution on account of pronounced influence of the secondary radiation, arising in the walls of the instrument, on the results of measurements. We used aluminum as the metal of lowest atomic weight and of most practical usefulness, as we intended to use the measure-

ments mostly for biologic experiments and biologic objects possess very low atomic weight. A knife switch, L, permitted charging the electrometer to the desired potential. The latter was the same as used in the other measuring instrument. The deflection of the gold leaf was observed by a reading microscope of large focus and provided with an ocular scale. The radio-active preparations under investigation were usually kept at a distance of 1 m. from the electrometer.

The secondary radiation, which originates in the walls of the work-room and the objects contained therein, is a source of error which must not be overlooked in the measurement of the intensity of radio-active substances. We reserved a large empty room solely for the purpose of measuring, thus to reduce the sources

FIG. 4.

of error to the smallest possible minimum. The apparatus was placed in the center of a wooden table.

We performed all our measurements of intensity with these two instruments. According to the definition of intensity we must determine the radiation energy striking upon a surface of 1 squ. cm. per second. The measurement of the energy of X-rays in an absolute measure, as is well known, offers almost unsurmountable difficulties. We, therefore, really cannot measure the energy, and hence also not the intensity with the instruments just described. We are only concerned with relative measurements of intensities in our biologic investigations. A comparative measurement of intensity is possible with such an instrument if the apparatus is always the same and if the details of the test remain the same. Amongst the latter may be mentioned, as one of the most important, the like qualities of the rays employed, as the measuring method does not permit comparison with each other of the intensity of rays of different qualities. This may be explained by the fact that a softer radiation ionizes stronger on account of greater

absorption by air than a harder radiation. The intensities may be otherwise alike.

### Measurement of Hardness of Rays

The hardness of X-rays in roentgen technique is measured according to different methods.

a. *The determination of hardness by the potential applied to the tube.*

This method uses the dependence of the hardness of rays on the potential of the tube. To this group belong:

1. The determination of hardness by the parallel spark-gap through which the electric current passes.

2. The sclerometer of Klingelfuss. It essentially depends on the fact that the mean tension, and therewith the mean tension in the tube, is determined by a voltmeter through the use of an accessory coil connected to the inductor.

3. The voltmeter of Bergonié and the qualimeter of Bauer measure the tension maintained at the tube, however, by electrostatic means in contradistinction to the sclerometer of Klingelfuss.

We could not use these methods for the determination of hardness of the rays as we employed almost exclusively filtered rays in our biologic investigations. However, they were used to obtain information about the conditions existing in the tube during its operation and about any change occurring in the tube during the observations. They were especially valuable with the Coolidge tube, because we were placed in a position to always regulate the tube to the desired degree of hardness and thus to control the quality of the rays during the course of a test.

b. *The determination of hardness by comparing the absorption of rays in two different metals.*

The Walter scale, the Wehnelt wedge and the Benoist scale are based on this method. The intensity of the rays which penetrate a silver leaf of a definite thickness is compared with the intensity of rays which pass through a block of aluminum of a wedge-shaped form by means of a fluorescent screen or a photographic plate.

We have not used these methods because they were not sufficiently sensitive for our experiments.

c. *Determination of the hardness by the half absorption value layer according to the method of Christen.*

The measurement of the half absorption value layer is carried out by Christen by comparing with a fluorescent screen the radiation reduced by a perforated lead plate to half its intensity with the radiation decreased in intensity by a bakelit step-ladder. The thickness of the layer of the bakelit penetrated is the half absorption value layer if the fluorescence is of the same intensity.

As valuable as the measuring method appears to be to enable one to quickly inform himself in an absolute value about the

penetrability of the radiation employed, it did not suffice for our purposes on account of the defective sensitiveness which depends on the difficulty in reading the results exactly.

d. *The determination of the hardness by measuring the intensity of the radiation at a given point before and after passing through a known layer of a known medium.*

This method, which is almost exclusively used in physics for the determination of the laws of absorption and the hardness, was employed by us in all experiments. We used the above-described measuring instruments and directions for the measuring of inten-

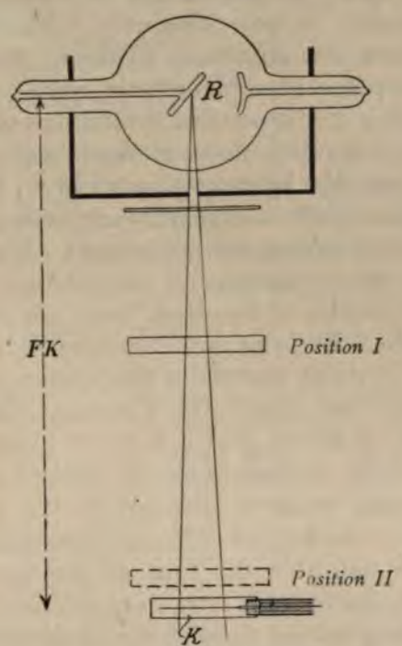


FIG. 5.

sity. Marked differences are frequently found recorded in literature if one compares the determinations of the penetrability of radiations obtained with these methods. These differences, when the X-rays are used, cannot be satisfactorily explained, as the data concerning the similarity of rays must be based on an absorption measurement. The quality of rays of the radio-active substances is defined by the substance. Absorption measurements of these therefore should always give the same results. The results, in this instance, also vary with the various investigators. They must be ascribed to essential differences in measuring instruments and to the details of the investigators with an otherwise identical method. This supposition may be easily confirmed by experimentation.

Arrangement of the test: The X-rays from a Coolidge tube R,

placed in a bowl lined with heavy leaded rubber, pass through an adjustable diaphragm. The small beam, thus obtained, strikes the ionization chamber K (see Fig. 5). The distance FK from the focus to the ionization chamber is 50 cm. The absorbing medium consists of a plate of aluminum 5 mm. thick. The plate can be adjusted within the limits of the radiation beam, so that at one time it is placed half-way between the focus and ionization chamber, and at the other time directly above the ionization chamber.

The course of the experiment is as follows: The tube is brought to the desired load and hardness by regulation of the hot filament current and the primary current of the inductor. The intensity of the ionization current is now measured without any absorbing medium. Thereupon the aluminum plate is placed in position I and the ionization current determined; the measurement is repeated without the absorbing medium; then the aluminum plate is adjusted to position II, and another measurement made. Then another measurement without the interposition of any absorbing material follows. It is thus possible to recognize any change in the hardness or intensity of X-rays during the experiment. We have made quite a number of such investigations.

The measuring results of two such tests are represented in the accompanying table. The one was performed with a voltage of a parallel spark-gap of 35 cm. and a filtration with aluminum of a thickness of 3 mm., the other with a voltage corresponding to a parallel spark gap of 40 cm. and a filter of 1 mm. copper.

In the first column is indicated the method of measuring. 0 refers to the time in which 5 divisions of the scale of the electrometer have been discharged without interposition of the aluminum plate. $Al_o$ indicates the time of the discharge when the aluminum plate is placed half way between focus and ionization chamber; while $Al_u$ gives the time of discharge when the aluminum plate is placed directly upon the chamber. The second and third columns give these time periods in seconds, the second column for the 3 mm. aluminum filtration, the third for the 1 mm. copper filtration.

| Method of Measuring | 3 mm. Aluminum: time in seconds | 1 mm. Copper: time in seconds |
|---|---|---|
| 0 | 15.2 | 19.4 |
| $Al_o$ | 29.2 | 25.8 |
| 0 | 15.0 | 19.2 |
| $Al_u$ | 25.6 | 23.4 |
| 0 | 15.2 | 19.8 |
| $Al_o$ | 29.4 | 26.8 |
| 0 | 14.8 | 20.5 |
| $Al_u$ | 25.0 | 25.8 |
| 0 | 15.0 | 21.0 |
| $Al_o$ | 28.8 | 27.8 |
| 0 | 15.2 | 20.2 |
| $Al_u$ | 25.8 | 24.4 |
| 0 | 15.0 | 19.8 |

The absorption may be calculated from the readings in per cent of the projected radiation.

| Method of Measuring | 3 mm. Aluminum | 1 mm. Copper |
|---|---|---|
| $Al._o$ | 48% | 25.5% |
| $Al._u$ | 41% | 21.5% |

We see from these tables that the location of the absorbing material has a marked influence on the result. The difference in per cent of the transmitted rays amounts to 14.5 per cent with the 3 mm. aluminum filtration and to 16 per cent with the 1 mm. copper filtration.

Quite a similar experiment was carried out with the gamma-rays of radium and mesothorium. The second measuring instrument was employed in these observations. A celluloid plate of a thickness of 5 mm. was placed in front of the electrometer exposed to the radiation source for the purpose of permitting only gamma-rays to strike the measuring chamber. The results, which were obtained with positions I and II of the absorbing medium (the same aluminum plate as used for the X-rays) are presented in the following table:

| Method of Measuring | 5 Units of Scale of Electrometer in seconds | | | Absorbed Radiation |
|---|---|---|---|---|
| 0 | 21.0 | 21.4 | 21.4 | Position I = 4.7% |
| Al. Position I | 22.4 | 22.2 | 22.6 | |
| 0 | 21.4 | 21.4 | 21.2 | Position II = 3.4% |
| Al. Position II | 22.2 | 22.0 | 22.0 | |
| 0 | 21.4 | 21.2 | 21.4 | |

Here also a remarkable dependence of the measured results on the position of the absorbing bodies is shown.

These differences in the results, according to whether the irradiated body is placed far from or near to the ionization chamber, must be explained by the secondary radiation which arises from the absorbing body. Naturally a larger portion of these secondary rays enters the ionization chamber if the absorbing body is placed immediately above it. The portion which is delivered by the secondary radiation for the intensification of the ionization, will be the greater, the closer the absorbing body is placed to the ionization chamber, and therefore a correspondingly smaller absorption is measured.

The measurements, just described, show that an exactly detailed description of the course of the experiment must be given in the determination of the absorption coefficient of a given quality of radiation in a given medium, and that only those results can be compared with each other which have been carried out under like

conditions. This also explains why the determinations of the degree of absorption of rays of the same quality in like bodies found recorded in literature differ.*

In the subsequent paragraphs we have always arranged the experiments for the determination of the degree of absorption in a known medium so that the radiated object was placed half way between the source of radiation and the measuring chamber.

*c. Determination of hardness by means of measuring the wave-lengths of the rays.*

Since the discovery of the interferences of crystals, whereby it is possible to dissect a roentgen or gamma radiation into its various wave-lengths, it has been proposed to employ this method to determine the wave-lengths characteristic of the hardness of a given radiation.

The hope often expressed that this method would be an exceedingly good and simple one for determining the quality of rays, has not been fulfilled as the method required quite a complicated apparatus, and the time to obtain a measurement, especially with filtered rays, might be too long.

## The Method of Measuring the Hardness of Rays Used in Our Experiments

We only used known components of radiation in our investigations of the biologic action of the various hard rays, as it is quite impossible to investigate all the components of the extensive X-rays spectrum and the radium spectrum as to their biologic action. Different kinds of hard rays are employed in radiation therapy to attain definite therapeutic results. They can be obtained by regulating the hardness of the tube and by using more or less strong filters. Filters of aluminum 3 to 10 mm. thick are mostly employed in deep therapy. We have used still stronger filters to produce rays, as hard as possible, as has also been done by other experimenters, Löwenthal, Wintz, etc.

We have not used aluminum as filtration material for the stronger filters, as filters of 15 to 20 mm. thickness are too unwieldy for practical use, but have chosen copper of 1 mm. thickness which corresponds to an aluminum filter of a 18 mm. thickness. We did not exceed the filter thickness of 1 mm. copper, because it is not possible to obtain a still greater hardening of the radiation with

* As will be seen from experiments cited in later chapters on the dependence of the time of application of a given dose on the size of the field, the position of the absorbing material does not alone play a rôle in the determination of the hardness of rays, but also the size of the employed radiation beam in relation to the measuring chamber. With the same measuring chamber the absorption coefficient is found the smaller, the larger the radiation beam is. The cause of the influence of the size of the radiation beam on the measuring result must be looked for in the secondary radiation originating in the absorbing body.

our present day instrumentarium, without causing a great economic loss.

The following radiation hardnesses are basic for our investigations:

### 1. *Unfiltered X-rays.*

We understand by unfiltered X-rays the rays arising from a Coolidge tube which is activated by an inductor and gas interruptor, so that the parallel spark-gap corresponds to a spark-gap of a length of 30 cm. measured between point and disc, while an accessory spark-gap of 5 cm. is placed in series with the tube.

We have measured the absorption curve of these rays in aluminum of 0 to 10 mm. thickness and in layers of water of 0—10 cm. thickness in order to gain a more detailed information on the hardness of the rays. We made use of the instrument for measuring described on page 9.*

We repeat as example an extract from the observation journal in order to give a true reproduction of the details of the measurement. In the following table, the method of measuring is placed in the first column. 0 indicates the time during which 5 units of the scale of the electrometer are passed without insertion of the absorbent aluminum in the radiation beam, 1 mm. aluminum, 2 mm. aluminum, and so forth, indicate the time duration of the discharge of 5 units of the scale, if a layer of aluminum of these thicknesses be inserted in the X-ray beam. The second column states the time in seconds. In the third column the intensity of the radiation after passing through the aluminum is expressed in per cent of the projected rays. In the last column the logarithm of this intensity is entered. The intensity of the radiation without the absorbing medium was always measured between each reading of the electrometer.

The graph (Fig. 6) gives the result if plotted.

*Extract from the observation journal.*

Hot cathode current = 3.45 ampères (applied to the cathode of Coolidge tube), of hot filament current of cathode of Coolidge tube.
Primary current = 6.5 ampères.
Secondary current = 3 milliampères.
Parallel spark gap = 30 cm. (unfiltered).
Filter = none.

* According to page 11, a comparative measuring of the intensity is only possible when rays of the same hardness are employed. For this reason the absorption curves subsequently recorded are, strictly speaking, not correct. The deviations from the straight line of the graphs of the unfiltered rays which may become considerably hardened in the layers of aluminum or water that serve the purpose of determining absorption, are only apparent ones. The filtered, especially the highly filtered, rays are much less changed in their hardness when passing through these layers.

| Way of Measurement Thickness of Aluminum in mm. | Time of Deflection of 5 Units of Scale of Electrometer in Seconds | | Intensity of Radiation in % of the Projected Radiation | Logarithm of Intensity |
|---|---|---|---|---|
| 0 | 10.4 | 10.6 | 100 | 2 |
| 1 | 15.6 | 15.2 | 68.6 | 1.84 |
| 0 | 10.4 | 10.8 | | |
| 2 | 20.2 | 20.1 | 51.3 | 1.71 |
| 0 | 10.4 | 10.6 | | |
| 3 | 26.2 | 26.2 | 39.9 | 1.60 |
| 0 | 10.4 | 10.4 | | |
| 4 | 32.8 | 31.8 | 32.4 | 1.51 |
| 0 | 10.6 | 10.4 | | |
| 5 | 35.8 | 35.0 | 29.0 | 1.46 |
| 0 | 10.4 | 10.6 | | |
| 6 | 42.4 | 41.4 | 25.4 | 1.40 |
| 0 | 10.8 | 10.8 | | |
| 7 | 50.4 | 47.6 | 21.7 | 1.34 |
| 0 | 10.8 | 10.2 | | |
| 8 | 55.8 | 52.4 | 19.4 | 1.29 |
| 0 | 10.4 | 10.4 | | |
| 9 | 64.8 | 61.4 | 16.8 | 1.23 |
| 0 | 10.6 | 10.8 | | |
| 10 | 71.2 | 70.8 | 15.0 | 1.18 |
| 0 | 10.4 | 10.6 | | |

We see from the values and from the deviation from the straight line of the graph obtained from the resultant measurements that it is possible to perform such measurements of X-rays with a

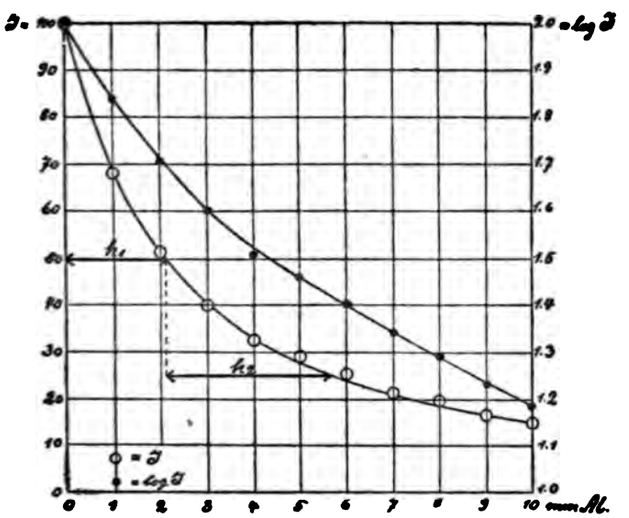

FIG. 6.—Absorption curve in aluminum of the "unfiltered X-rays" applied according to directions given.

considerable exactness within range of a small percentage of error. The first half absorption value layer of unfiltered rays, measured in aluminum, amounts to 2.15 mm. while the second half absorption value layer is 3.55 mm. The first half absorption value layer is thus considerably smaller than the second one, and the

radiation is therefore very non-homogeneous. The measurement of heterogeneity according to Christen is $h_2 : h_1 = 3.55 : 2.15 = 1.65$. The heterogeneity may be graphically shown if the intensity is plotted logarithmically. The graph forms a straight line for a homogeneous radiation in which the absorption progresses according to simple exponential laws. In our example the logarithmic graph is strongly curved, indicating a marked non-homogeneity.

We used aluminum as an absorption medium because it is the custom in physics. We, also, have measured the absorption in water for reasons which will be explained in the chapter "Measuring of Dose." The first half absorption value layer in water is 1.8 cm., the second half absorption value layer 2.25, as may be seen in the following table and Fig. 7.

| Thickness of Layer of Water in cm. | Intensity of Radiation in % of the Projected Radiation | Logarithm of Intensity |
|---|---|---|
| 0 | 100 | 2.00 |
| 1 | 68 | 1.83 |
| 2 | 46 | 1.66 |
| 4 | 24 | 1.38 |
| 6 | 14 | 1.15 |
| 8 | 8 | 0.90 |
| 10 | 4.5 | 0.65 |

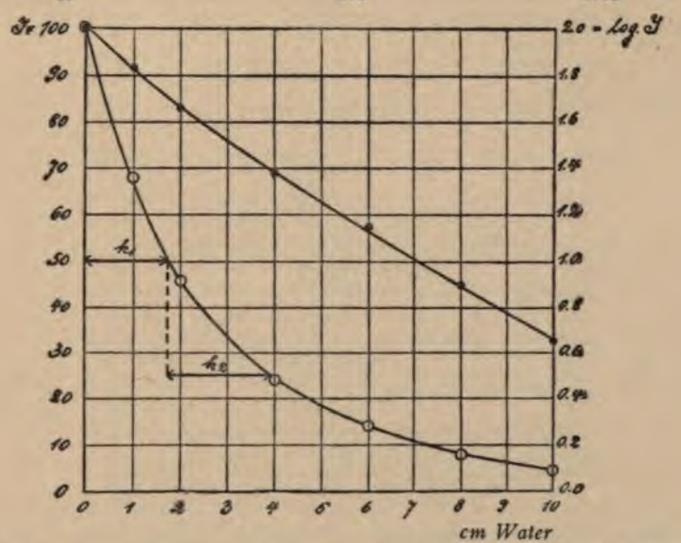


FIG. 7.—Absorption curve in water of unfiltered rays obtained according to directions.

The heterogeneity, therefore, is $h_2 : h_1 = 2.25 : 1.8 = 1.25$. The logarithmic graph also shows the marked deviation from a straight line.

### 2. *X-rays Filtered with 3 mm. Aluminum.*

X-rays filtered with 3 mm. aluminum are rays emitted from a Coolidge tube which is operated with an inductor and gas inter-

rupter so that the potential measured between point and disc corresponds to a parallel spark-gap of a length of 30 cm., while an accessory spark-gap of 5 cm. is placed in series with the tube. The rays pass through a sheet of aluminum 3 mm. thick before they strike the object to be radiated. The behavior of the absorption of these rays in aluminum and in water is presented in the two following tables and Figs. 8 and 9. The results have been obtained with the same arrangement and method of measuring as adopted in the experiments with unfiltered rays.

| Thickness of Aluminum | Intensity of Radiation in % of Projected Radiation | Logarithm of Intensity |
|---|---|---|
| 0 | 100 | 2.0 |
| 1 | 82.3 | 1.92 |
| 2 | 70.4 | 1.85 |
| 3 | 59.2 | 1.77 |
| 4 | 51.4 | 1.71 |
| 5 | 47.5 | 1.68 |
| 6 | 41.6 | 1.62 |
| 7 | 37.0 | 1.57 |
| 8 | 33.5 | 1.53 |
| 9 | 30.1 | 1.48 |
| 10 | 26.6 | 1.42 |

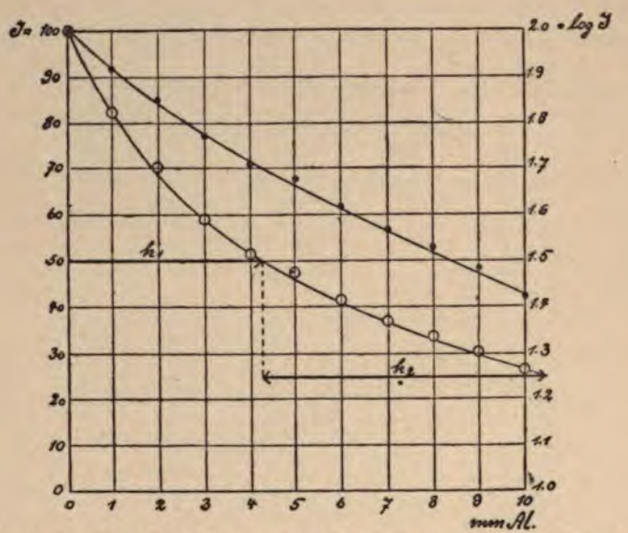


FIG. 8.—Absorption curve in aluminum of X-rays filtered through 3 mm. of aluminum applied as directed.

We observe from the graph in Fig. 8 that the radiation has become harder by filtration through 3 mm. aluminum. The first half absorption value layer is 4.25 mm. and the second half absorption value layer 6.25 mm. We also note that the rays filtered through 3 mm. aluminum show a considerable difference between the two half absorption value layers; therefore the radiation is still non-homogeneous.

The heterogeneity is $h_2 : h_1 = 6.25 : 4.25 = 1.47$.

An improvement in the heterogeneity may be also observed from the logarithmic graph, which does not exhibit such a marked curving as the logarithmic graph of the unfiltered radiation.

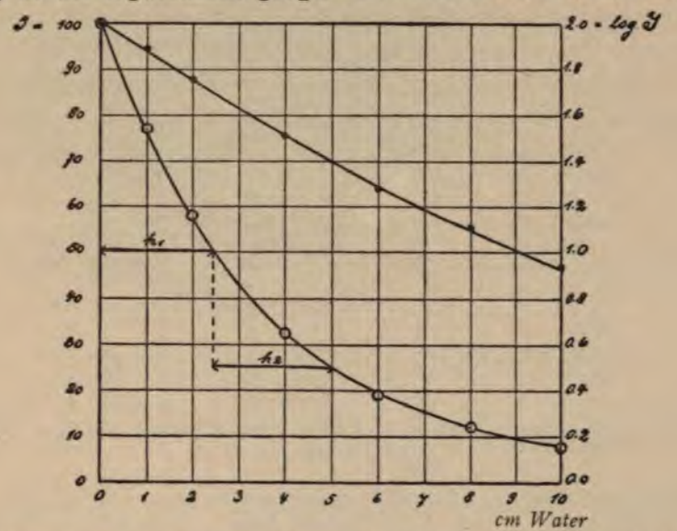


FIG. 9.—Absorption curve in water of X-rays filtered through 3 mm. aluminum applied as directed.

| Thickness of Layer in Water in cm. | Intensity of Radiation in % of Projected Rays | Logarithm of Intensity |
|---|---|---|
| 0 | 100 | 2.00 |
| 1 | 77 | 1.89 |
| 2 | 58 | 1.76 |
| 4 | 32.5 | 1.51 |
| 6 | 19.0 | 1.28 |
| 8 | 12.0 | 1.01 |
| 10 | 8.7 | 0.94 |

From the table and graph in Fig. 9 the first half absorption value layer in water is 2.4 cm. and the second 2.65 cm. The heterogeneity is $h_2 : h_1 = 2.65 : 2.4 = 1.1$ cm.

### *3. X-rays Filtered with 10 mm. Aluminum.*

X-rays filtered with 10 mm. aluminum are rays arising from a Coolidge tube, operated with an inductor and gas interrupter, so that the potential corresponds to a parallel spark-gap of a length of 35 cm. measured between point and disc, while an accessory spark-gap of 5 cm. is inserted in series with the tube.

The rays pass through a filter of 10 mm. aluminum before striking the object to be radiated. The course of the absorption of these rays in aluminum and in water is represented in the two following tables and Figs. 10 and 11. The results have been obtained with the same details and methods of measuring used in the preceding absorption measurements.

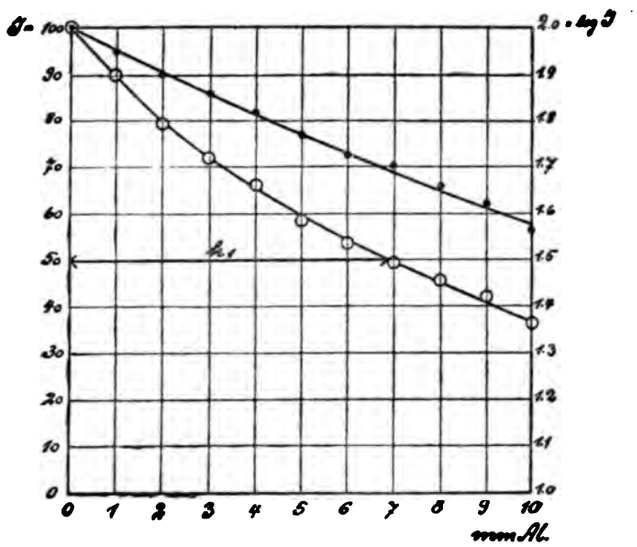


FIG. 10.—Absorption curve in aluminum of X-rays filtered through 10 mm. aluminum and applied as directed.

| Thickness of Aluminum in mm. | Intensity of Radiation in % of Projected Rays | Logarithm of Intensity |
|---|---|---|
| 0 | 100 | 2.00 |
| 1 | 90.0 | 1.95 |
| 2 | 79.4 | 1.90 |
| 3 | 72.4 | 1.86 |
| 4 | 66.4 | 1.82 |
| 5 | 58.9 | 1.77 |
| 6 | 54.1 | 1.73 |
| 7 | 49.8 | 1.70 |
| 8 | 45.9 | 1.66 |
| 9 | 42.1 | 1.62 |
| 10 | 36.2 | 1.56 |

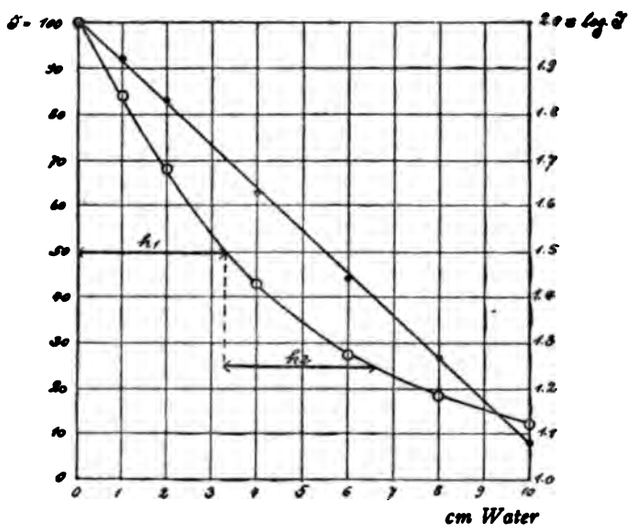


FIG. 11.—Absorption curve in water of X-rays filtered through 10 mm. aluminum and applied according to directions.

We note from the graph of Fig. 10 that the radiation after passing through an aluminum filter of 10 mm. thickness has grown still harder than the radiation filtered with 3 mm. aluminum. The first half absorption value layer measures 6.9 mm. The thickness of 10 mm. aluminum does not suffice for the determination of the second half absorption value layer. The greater homogeneity of the rays filtered through 10 mm. aluminum in contradistinction to that of the rays filtered with 3 mm. aluminum may be recognized from the logarithmic graph which almost approaches a straight line.

| Thickness of Layer of Water, in cm. | Intensity of Radiation in % of Projected Rays | Logarithm of Intensity |
|---|---|---|
| 0 | 100 | 2.00 |
| 1 | 84 | 1.90 |
| 2 | 68 | 1.83 |
| 4 | 43 | 1.63 |
| 6 | 27.5 | 1.44 |
| 8 | 18.5 | 1.27 |
| 10 | 12.0 | 0.60 |

The first half value absorption layer in water obtained from table and Fig. 11, is 3.25 cm., the second half absorption value layer 3.3 cm. The heterogeneity is $h_2 : h_1 = 3.3 : 3.25 = 1.02$ cm. The logarithmic graph also approaches the straight line.

### 4. *X-rays Filtered with 1 mm. Copper.*

X-rays filtered with 1 mm. copper are rays which start from a Coolidge tube, operated with an inductor and gas interrupter so

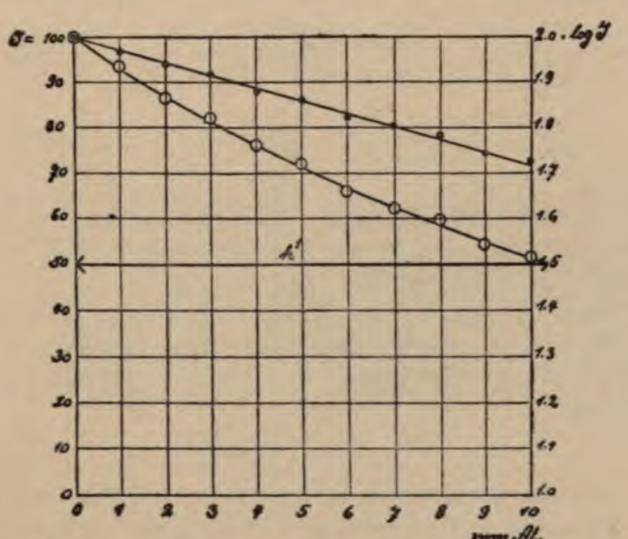


FIG. 12.—Absorption curve in aluminum of X-rays filtered through 1 mm. of copper and applied according to directions.

that the potential corresponds to a parallel spark-gap of 40 cm. measured between point and disc, while an accessory spark-gap of 5 cm. is inserted in series with the tube.

The rays are filtered through a layer of 1 mm. copper before striking the object to be radiated. The progress of the absorption of these rays in aluminum and in water is reproduced in the two following tables and Figs. 12 and 13. The results have been obtained with the same details and method of measuring as used in the absorption measurements of the unfiltered rays.

| Thickness of Aluminum in mm. | Intensity of Rays in % of Projected Rays | Logarithm of Intensity |
|---|---|---|
| 0 | 100.0 | 2.00 |
| 1 | 93.9 | 1.97 |
| 2 | 86.8 | 1.94 |
| 3 | 82.3 | 1.92 |
| 4 | 76.5 | 1.88 |
| 5 | 72.1 | 1.86 |
| 6 | 66.0 | 1.82 |
| 7 | 62.7 | 1.80 |
| 8 | 60.0 | 1.78 |
| 9 | 54.0 | 1.74 |
| 10 | 53.6 | 1.73 |

We see from the graph in Fig. 12 that the rays have become still harder after passing through a filter of 1 mm. copper. The first half value absorption layer is 1.05 mm. The course of the logarithmic graph may be considered as approaching a straight line.

| Thickness of Layer of Water, in cm. | Intensity of Rays in % of Projected Rays | Logarithm of Intensity |
|---|---|---|
| 0 | 100 | 2.00 |
| 2 | 70 | 1.86 |
| 4 | 47 | 1.67 |
| 6 | 31 | 1.49 |
| 8 | 22.5 | 1.35 |
| 10 | 15 | 1.18 |

From the table and Fig. 13 we obtain the first half value absorption layer in water of 3.7 cm. and the second of 3.75 cm. The heterogeneity is $h_2 : h_1 = 3.75 : 3.7 = 1.01$.

This value being close to 1 demonstrates that this ray already approaches a homogeneous radiation. The logarithmic graph is a straight line and corresponds to an almost perfect homogeneity of radiation.

### *5. Gamma-Rays.*

We generally understand by gamma-rays the rays from radioactive substances which have passed a brass filter of 1.5 mm. thickness and an additional filter of 5 mm. celluloid. The celluloid serves the purpose of absorbing the secondary radiation formed

in the brass filter. The first half absorption value layer of gamma-rays of radium according to the described method of measurement is 48 mm. and that of mesothorium 52 mm. The half absorption value layers do not differ considerably. If we compare them with the half absorption value layers of the hardest filtered X-rays we use, we see that this half absorption value layer is quite considerably larger.

The combined gamma-rays of radium and mesothorium were employed in part of the biologic investigations, as some of the latter required a large amount of radio-active substances which we did not possess in either one of the individual preparations. We also employed other filters than brass, and also other filters

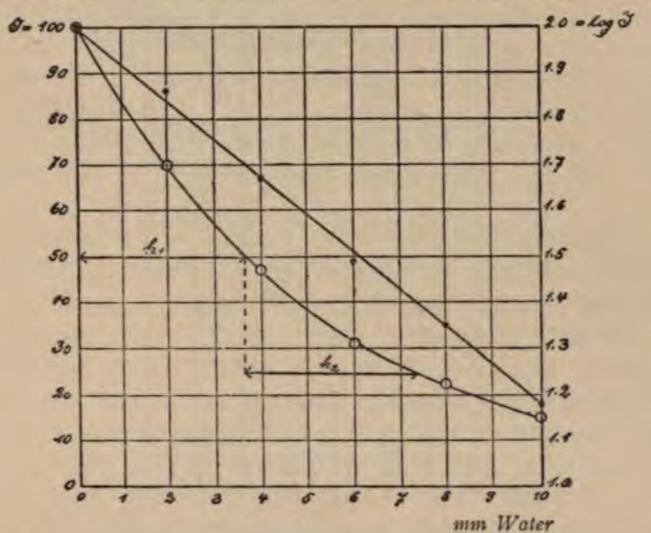


FIG. 13.—Absorption curve in water of X-rays filtered through 1 mm. of copper, applied as directed.

than celluloid for the absorption of the Sagnac rays in some of our investigations. The composition of the rays filtered with special filters has been recorded in the respective chapters of the biologic section.

If we collectively compare the rays of different hardnesses, which we employ, and if we place them graphically side by side (see Fig. 14), we see that the differences in the degrees of hardness are considerable. Quite important differences even exist between the various highly filtered X-rays. A great difference especially is seen between the half absorption value layer of the gamma-rays of radium and mesothorium and the highest filtered X-rays. The statement is often found in literature that the new X-ray apparatuses deliver radiations that almost equal the gamma-rays in hardness. As a matter of fact, X-rays of the same hardness as gamma-rays do exist because the range of hardness of

gamma-rays of the various products of radio-active decay is wide. The penetrability of gamma-rays of mesothorium and radium, that are solely used in deep therapy, has never been attained with the X-rays.

In the chapter on measuring hardness we shall see that comparative values only can be obtained when we observe the same details in the experiments and use the same methods of measurement. We have not been able to find in the literature comparative measurements that could pass a critical investigation, as authors

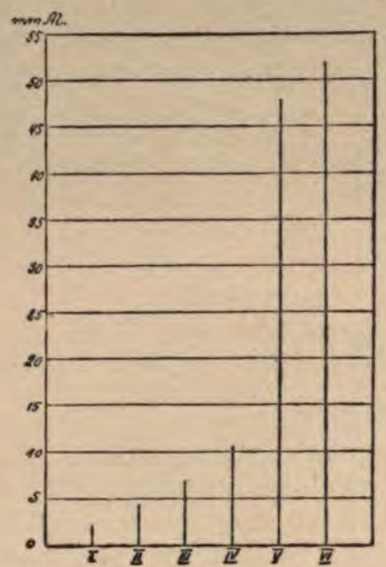


FIG. 14.

The first half value absorption layers in mm. of aluminum

I. For unfiltered X-rays.
II. For X-rays filtered through 3 mm. of aluminum.
III. For X-rays filtered through 10 mm. of aluminum.
IV. For X-rays filtered through 1 mm. of copper.
V. For radium rays filtered with 1.5 mm. brass and 5 mm. celluloid.
VI. For mesothorium rays filtered with 1.5 mm. brass and 5 mm. celluloid.

who have been interested in the measurement of X-rays mostly record in these comparisons the measured results of gamma radiations made by others.

We cite in the following a few experiments which we carried on to compare the penetrations of X-rays filtered with 1 mm. copper and the gamma-rays of radium. We used the measuring instrument described on page 10. In the experiments with X-rays the point source of radiation of the anticathode was placed at the same distance (i.e., 1 meter) from the electrometer as in those with the gamma-rays of radium preparations. The absorbing material in both instances was directly placed before the electrometer. This

position of the absorbing filter appeared to us less objectionable than the location of the absorption medium close to the source of radiation. The beta-rays formed in the furnishings and walls of the work-room present a considerable source of error in the measurements, and cause the hardness to be measured too high. These undesirable radiations, however, may be excluded from the measuring chamber by placing the absorbing filter close to the electrometer. We performed the determination of the half absorption value layer in aluminum. The details of the experiment followed closely those for the measurement of hardness described in detail on page 19. The intensity of the total radiation was always determined before and after a passage through the absorbing medium. From the experiments we obtained a first half absorption value layer of 16.5 mm. in aluminum for X-rays filtered with 1 mm. copper, and a half absorption value layer of 58 mm. of aluminum for gamma-rays of radium filtered with 1.5 mm. brass plus 5 mm. celluloid.

The half absorption value layer of X-rays filtered with 1 mm. copper and that of "gamma-rays" of radium are in a ratio of 1 : 3.5.

In the literature of physics the absorption coefficient and the half absorption value layer of X-rays are usually given in aluminum, on the other hand those with gamma-rays are given in lead as the absorbent. It appeared to us of interest to test the half absorption value layer of our hardest X-rays in both these absorbing materials using the same method of investigation. This point has been sorely neglected, as seen in the literature in which the values of the half absorption value layers of filtered X-rays and gamma-rays are reported which were obtained in aluminum for X-rays and in lead for gamma-rays, two substances widely different in atomic weight and density. The results are compared by arithmetical corrections. Naturally such methods of comparison are fraught with great errors.

The method of measuring described on page 10 was used in these investigations. The radium preparation was placed at a distance of 1 meter from the ionization chamber when measuring absorption of the gamma-rays; the anticathode of the Coolidge tube which was placed in a bowl was also placed 1 meter from the ionization chamber for the measurement of the absorption of X-rays. The X-radiation beam was by means of a diaphragm chosen so large that the ionization chamber was completely enclosed by it. The absorbing material was placed directly in front of the ionization chamber with both radiations. The course of the experiment was otherwise the same as that in the preceding absorption measurements.

In the following tables two series of measurements are recorded in which the absorptions in 10 mm. aluminum and 1 mm. lead respectively are considered.

X-RAYS FILTERED WITH 1 MM. COPPER

| Method of Measuring | Time of Deflection of 5 Units of the Scale of Electrometer, in seconds | Intensity of Rays in % of Projected Rays |
|---|---|---|
| 0 | 9.8 | |
| 10 mm. aluminum | 16.0 | |
| 0 | 9.6 | For aluminum |
| 1 mm. lead | 61.0 | =64.6% |
| 0 | 10.2 | With correction=66.2% |
| 10 mm. aluminum | 15.8 | |
| 0 | 10.6 | |
| 1 mm. lead | 62.0 | For lead |
| 0 | 10.2 | =16.7% |
| 10 mm. aluminum | 15.6 | With correction=16.3% |
| 0 | 10.4 | |
| 1 mm. lead | 60.0 | |
| 0 | 10.4 | |

GAMMA RAYS OF RADIUM FILTERED WITH 1.5 MM. BRASS AND 5 MM. CELLULOID

| Method of Measuring | Time of Deflection of 5 Units of Scale of Electrometer, in seconds | Intensity of Rays in % of Projected Rays |
|---|---|---|
| 0 | 48.8 | |
| 10 mm. aluminum | 54.6 | |
| 0 | 49.0 | |
| 1 mm. lead | 54.4 | For aluminum |
| 0 | 49.2 | =90.2% |
| 10 mm. aluminum | 54.6 | |
| 0 | 49.0 | |
| 1 mm. lead | 54.4 | |
| 0 | 48.8 | For lead |
| 10 mm. aluminum | 54.2 | =90.2% |
| 0 | 49.2 | |
| 1 mm. lead | 54.8 | |
| 0 | 49.0 | |

The conclusions to be drawn from both series of measurements are that lead absorbs X-rays much more than it does gamma-rays, as many gamma-rays pass 1 mm. lead as pass 10 mm. aluminum, while 1 mm. lead absorbs more X-rays filtered with 1 mm. copper than do 30 mm. aluminum.

We see from these series of measurements that a marked difference in penetration exists between the hardest X-rays and the gamma-rays. The point might be raised that our X-rays filtered with 1 mm. copper were not of the same hardness as the X-rays used by other experimenters in their comparisons of X-rays and gamma-rays, and that their radiations were essentially harder. This seems to be improbable, as we were not in a position to observe a still further increase in the hardness of rays when using a filter even heavier than 1 mm. copper. The parallel spark-gap of 40 cm. is a potential representing the limit of present possibilities.

The ratio of the two first half absorption value layers and the deflection of the logarithmic absorption graph from the straight line must be considered as the measurements of homogeneity.

In the following table the quotients of the first two half absorption value layers measured in water of all the rays used by us have been compiled, and in Fig. 14A the four logarithmic absorption graphs for aluminum have been plotted.*

We may conclude that the graphs of the unfiltered X-rays and X-rays filtered with 3 mm. aluminum materially differ from a straight line, but that the graphs of the X-rays filtered with 10 mm. aluminum already approach a straight line. The graph of X-rays

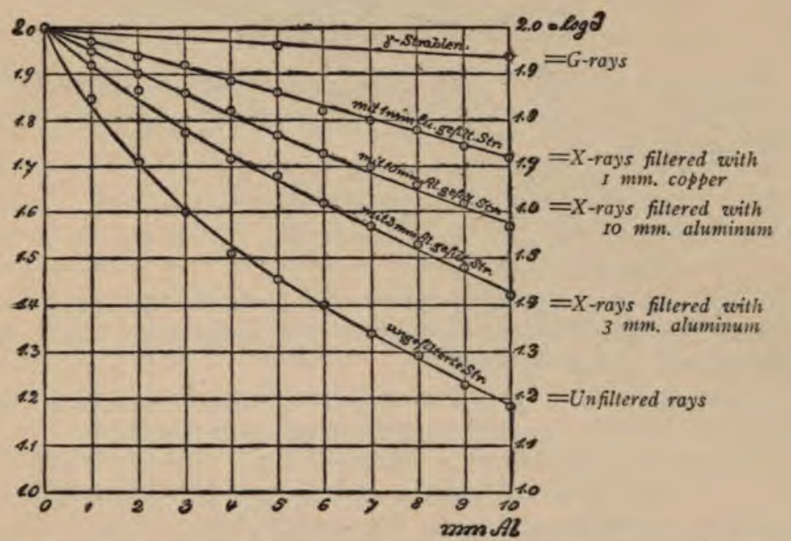
2.0 = Log J
γ-Strahlen.
=G-rays
mit 1 mm Al. gefilt. Str.
=X-rays filtered with 1 mm. copper
mit 10 mm Al gefilt. Str.
=X-rays filtered with 10 mm. aluminum
mit 3 mm Al gefilt. Str.
=X-rays filtered with 3 mm. aluminum
ungefilterte Str.
=Unfiltered rays
2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0
0 1 2 3 4 5 6 7 8 9 10
mm Al

FIG. 14a.—Logarithmic absorption curves of the radiations investigated by us.

filtered with 1 mm. copper may be considered a straight line. X-rays filtered with 1 mm. copper therefore may be assumed to be homogeneous.

A great importance is ascribed to the interpretation of homogeneity in literature. The views concerning the definition diverge considerably. We may be permitted to state that the method of the analysis of the absorption of radiations for the determination of homogeneity only gives approximate values. The method of spectral analysis gives more exact information about the dispute whether a radiation is homogeneous or heterogeneous. We also have employed the method of spectral analysis for this purpose and have examined all varieties of unfiltered and filtered radiations by the absorption analysis as well as by the spectral analysis. We will consider a spectrum obtained from X-rays filtered with 1 mm.

* The graph for gamma-rays has been entered for comparison.

copper. We cannot prove heterogeneity by means of the absorption analysis. The spectrum shows that a considerable range of wavelengths is present. Therefore the X-rays filtered with 1 mm. copper are still markedly heterogeneous. We justly doubt that such a minute and detailed analysis of homogeneity of a radiation is of any importance for the practice of radiation therapy. The method of the absorption analysis appears to suffice completely.

With this method, we cannot recognize a deviation of the logarithmic absorption graph from the straight line or if the quotient of the first half absorption value layers is close to 1, then the radiation must be considered as practically homogeneous.

## Measuring the Dose

We defined as unit of dose the radiation energy absorbed in a unit volume, i.e., in 1 ccm. of the biologic object and expressed it in the formulæ

$$D = \frac{E_1 - E_2}{V} \text{ or } D = \frac{F}{h} = \frac{J \cdot t}{h}$$

It has not been possible up to the present time to directly measure this quantity, because in such a measurement two presuppositions must be fulfilled:

1. The test object subjected to the action of radiations must become measurably changed by the influence of the rays.

2. The test object must possess the same laws of absorption for the various kinds of rays as the biologic body in which the applied dose is to be measured. Only thus is the energy absorbed in the unit volume of the test object equal to the energy absorbed in the unit volume of the biologic object.

We do not at present possess such a test object. As desirable as it may be to know the absorbed energy in an absolute measure to gain an idea of the nature of the biologic reaction and the transformation of energy therein, it is only necessary in biologic investigations to compare known doses with each other; a relative measure suffices. We may attain this relative measure with the customary dosimeters, such as the Kienböck strips, the Sabouraud Noiré tablets, the Fürstenau intensimeter, and lastly the ionometers. Definite, though different reactions from the action of rays appear in the measuring media of these dosimeters. The degree of the reaction depends naturally on the energy absorbed and therefore also on the surface energy of the rays striking the test body and on the absorption taking place in the test body. As the dose in the biologic object is also dependent on the surface energy and the absorption, so the degree of reaction in the test body is proportional to the dose in the biologic object. However, these conditions

obtain only there if we deal with one and the same hardness of radiation. If we intend to compare doses with each other that have been applied with radiations of different penetrabilities, or that have been applied with rays of varying heterogeneity, then the above deliberations hold good only if the laws of absorption are the same in the test body and in the biologic object, or at least if the ratio of the degrees of absorption in the test body and in the biologic object is constant for the different hardnesses of radiations.

In the following the ratio of the degrees of absorption in the various reactive substances to the degree of absorption in the biologic object has been determined with varying hardnesses of rays in order to gain from the difference in the ratios obtained a knowledge of the magnitude of the errors with the different test objects used in the dosimeters mentioned above.

The biologic object, in our case the human or animal body, consists of substances of varying densities, but they all have one thing in common, they are composed of elements of lowest atomic weight. The bones are an exception due to the content of calcium. These tissue layers of the human body play an important rôle in the absorption of rays. They are muscle, fat and bone.

We next investigated the question, whether these three substances have such slight deviations in their absorption, that the differences might be negligible. Though investigations on these factors have been recorded in literature we deemed it necessary to again compare the degree of absorption of the different hard rays in fat, muscle and bone tissue. The method of procedure in these investigations was the same as given on page 9.

The tissues to be examined, as muscle, fat and bone were ground to a pulp in a meat and bone grinder. To give these pulps a definite shape and size they were put in rectangular boxes of celluloid of a wall thickness of 1 mm. and a height of 5 cm. The thickness of the layers of these three substances corresponded to their density. A definite height could be produced with a sufficient exactness on account of the uniform fineness of the ground substance. It amounted to 35 mm. for these experiments. The same method and course of the measuring was followed as described in the preceding tests. Therefore we will only record the results of the measurements. We used X-rays either unfiltered, or filtered with 3 mm. aluminum, 10 mm. aluminum and 1 mm. copper, and gamma-rays of radium or mesothorium preparations of 50 mg. radium element activity.

We may deduce from the following table that a certain difference of absorption exists between muscle and fat on the one hand, and bone substance on the other. However, the differences between muscle and fat tissues are so slight that muscle tissue may be considered generally as an average biologic object.

| Hardness of Rays | Absorbed Radiation in % of Projected Rays | | |
|---|---|---|---|
| | Muscle | Fat | Bones |
| Unfiltered X-rays ..... | 74.6% | 63.4% | 87.0% |
| X-rays filtered with 3 mm. aluminum..... | 63.4% | 54.0% | 73.8% |
| X-rays filtered with 10 mm. aluminum..... | 55.0% | 44.6% | 62.8% |
| X-rays filtered with 1 mm. cu..... | 47.5% | 40.8% | 53.4% |
| Gamma-rays..... | 16.7% | 15.4% | 17.4% |

As it would be very inconvenient to compare the absorption of the reagent in the test object always with muscle tissue, we further determined whether the more easily accessible water has properties of absorbability equal to those of muscle tissue. Water, like muscle tissue, is composed of elements of lowest atomic weight and therefore has been frequently used for comparisons.

*Comparison of Absorption between Muscle Tissue and Water.*

Celluloid boxes of a wall thickness of 1 mm. and a height of 5 cm. were also used for these experiments. Distilled water 5 cm. in height and ground meat 5 cm. in thickness were used for the measuring.

We extended the investigations to the different varieties of hardnesses of rays, i.e., X-rays, unfiltered; filtered with 3 mm. aluminum, 10 mm. aluminum and 1 mm copper; and gamma-rays of mesothorium and radium filtered with 1.5 mm. brass plus 5 mm. celluloid.

The results have been collected in the following table:

| Hardness of Rays | Absorption in 5 cm. of Water | Absorption in 5 cm. of Meat | Proportion of Absorption in 5 cm. of Water to Absorption in 5 cm. Meat |
|---|---|---|---|
| Unfiltered X-rays ..... | 80.6% | 81.6% | 0.99 |
| X-rays filtered with 3 mm. al.. | 68.4% | 70.0% | 0.98 |
| X-rays filtered with 10 mm. al. | 63.4% | 65.4% | 0.98 |
| X-rays filtered with 1 mm. cu.. | 57.7% | 59.5% | 0.97 |
| Gamma-rays of mesothorium filtered with 1.5 mm brass + 5 mm. celluloid ..... | 21.5% | 22.7% | 0.95 |

The values were obtained from a series of experiments; the mean of the readings on the electrometer was always taken. The degree of exactness of the measurements was considerably high on account of using a Coolidge tube.

We see from the table that the absorption in 5 cm. water differs only slightly from that in 5 cm. muscle tissue. The fact that the ratio of absorption in muscle and water is constant for the various degrees of hardness used may permit us to neglect the slight difference, so that instead of muscle we may use water in the measurements of absorption. Water serves in certain respects as a basis for the measurement of absorption in the biologic object.

As water offers in certain experimentations difficulties on account of its liquid state, Perthes had to employ a solid substance,

namely aluminum, as phantom material. He has shown that 1 mm. aluminum absorbs almost as great an amount of X-rays as 1 cm. of body tissue. These aluminum phantoms have found general use in practice on account of their convenience. Perthes' investigations were performed with relatively soft rays. The question arose whether these comparative determinations also hold good for our experimentations in which we employ considerably harder radiations.

Christen has already pointed to the fact that aluminum deviates in its characteristics from those of water if stronger filters are used. The absorption in water and therefore muscle is smaller than would be expected according to the calculations made in the aluminum phantom.

We determined the deviations due to the hardnesses of rays considered in our experiments and record the same in the following table. We compared the absorption in a layer of water of 5 cm. placed in a celluloid box with that of an aluminum plate of 5 mm. thickness. We used the same quality of rays as in the preceding tables, and added another quality of radiation, in order to show that the measurements obtained with the soft ray conform to those of the investigations of Perthes.

| Hardness of Rays | Absorption in Water | Absorption in Aluminum | Al/W |
|---|---|---|---|
| Unfiltered rays spark gap 20 cm..... | 82.7% | 75.1% | 0.91 |
| Unfiltered rays spark gap 30 cm..... | 81.1% | 70.2% | 0.87 |
| X-rays filtered with 3 mm. aluminum..... | 71.8% | 53.4% | 0.74 |
| X-rays filtered with 10 mm. aluminum..... | 62.4% | 37.3% | 0.60 |
| X-rays filtered with 1 mm. cu. ..... | 58.7% | 28.2% | 0.48 |
| Gamma-rays of radium resp. mesothorium filtered with 1.5 mm. brass + 5 mm. celluloid..... | 22.7% | 6.3% | 0.28 |

The table confirms the opinion of Christen and shows that we cannot use the aluminum phantom in our investigations on the hardnesses of rays we employ. The differences in the ratios of absorption in aluminum and muscle or water are too great.

*Investigations about the Reagents used in the Test Objects.*

We have tested the ratio of the degree of absorption in the different reagents of the dosimeters to that of absorption in water with varying hardnesses of rays to obtain an idea of the extent of the discrepancies existing due to the reagents. This we could do as the biologic object may be replaced by the water phantom.

*Comparison of Absorption in Silver and in Water.*

The essential reacting substance in the Kienböck strips is, besides the bromine and chlorine, the silver contained in the photographic film. To obtain an exact measure of the size of error of this test substance we determined the absorption in silver and

water with the various qualities of rays employed by us. We compared the absorption in 5 cm. of water with that in a sheet of silver 0.1 mm. thick. The results are contained in the following table *

COMPARISON OF ABSORPTION OF X- AND GAMMA-RAYS IN WATER AND SILVER

| Hardness of Rays | Method of Measur'g | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Silver | Silver to Water |
|---|---|---|---|---|---|
| | 0 | 10.2 | | | |
| | Water | 35.2 | | | |
| | 0 | 11.0 | | | |
| | Silver | 29.2 | | | |
| | 0 | 11.0 | 69.4% | 63.5% | 0.92 |
| | Water | 35.0 | with | with | with |
| Unfiltered | 0 | 11.4 | correction | correction | correction |
| X-rays | Silver | 30.4 | for the | for the | 0.93 |
| | 0 | 10.4 | insulation | insulation | |
| | Water | 36.0 | error | error | |
| | 0 | 10.6 | 79% | 73% | |
| | Silver | 30.2 | | | |
| | 0 | 11.2 | | | |
| | Water | 35.0 | | | |
| | 0 | 11.2 | | | |
| | 0 | 12.4 | | | |
| | Water | 26.4 | | | |
| | 0 | 12.6 | | | |
| | Silver | 24.0 | | | |
| | 0 | 12.6 | 53.5% | 48.1% | 0.91 |
| | Water | 27.2 | with | with | with |
| X-rays filtered | 0 | 12.6 | correction | correction | correction |
| with 3 mm. | Silver | 24.4 | for the | for the | 0.91 |
| aluminum | 0 | 12.4 | insulation | insulation | |
| | Water | 27.0 | error | error | |
| | 0 | 12.6 | 62% | 56% | |
| | Silver | 24.2 | | | |
| | 0 | 12.6 | | | |
| | Water | 27.8 | | | |
| | 0 | 12.6 | | | |
| | 0 | 11.4 | | | |
| | Water | 29.2 | | | |
| | 0 | 12.0 | | | |
| | Silver | 21.2 | | | |
| | 0 | 11.0 | | | |
| | Water | 28.2 | | | |
| X-rays filtered | 0 | 11.6 | | | |
| with 10 mm. | Silver | 22.4 | 59.5% | 45.8% | 0.77 |
| aluminum | 0 | 11.8 | | | |
| | Water | 29.0 | | | |
| | 0 | 11.8 | | | |
| | Silver | 21.2 | | | |
| | 0 | 12.0 | | | |
| | Water | 29.2 | | | |
| | 0 | 12.0 | | | |

* Some of the measurements were carried on during a period of severe rains in summer-time. The insulation of the measuring instrument seems to be less efficient in a damp atmosphere. Therefore, corresponding corrections for the loss of insulation had to be made, that were unnecessary in the other measurements made at more favorable seasons of the year.

| Hardness of Rays | Method of Measur'g | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Silver | Silver to Water |
|---|---|---|---|---|---|
| | 0 | 11.0 | | | |
| | Water | 21.6 | | | |
| | 0 | 11.4 | | | |
| | Silver | 15.4 | | | |
| | 0 | 11.4 | 49.7% | 26.6% | 0.54 |
| | Water | 22.0 | with | with | with |
| X-rays filtered | 0 | 11.2 | correction | correction | correction |
| with 1 mm. cu. | Silver | 14.8 | for the | for the | 0.51 |
| | 0 | 11.2 | insulation | insulation | |
| | Water | 22.0 | error | error | |
| | 0 | 11.8 | 56.5% | 29.0% | |
| | Silver | 15.4 | | | |
| | 0 | 12.0 | | | |
| | Water | 23.2 | | | |
| | 0 | 12.0 | | | |
| | 0 | 21.4 21.4 21.6 | | | |
| | Water | 27.8 27.8 28.0 | | | |
| Gamma-rays | 0 | 21.6 21.8 21.6 | 22.4% | very small | very small |
| | Silver | 21.6 21.6 21.8 | | | |
| | 0 | 21.4 21.4 21.6 | | | |

We see from this table that quite marked differences exist in the ratios of the amount of absorption in water and in silver with the different qualities of rays.

*Comparison of Absorption in Water and in Platinum.*

Platinum, besides barium, serves as the reagent in the Sabouraud-Noiré tablets. In order to obtain a measure for the magnitude of the error of this test object we determined the absorption in platinum and in water for the different hardnesses of rays in the same manner as with silver. We compared the absorption in 5 cm. of water with that in a sheet of platinum of a thickness of 0.03 mm. The results are contained in the following table

COMPARISON OF ABSORPTION OF X- AND GAMMA-RAYS IN WATER AND PLATINUM

| Hardness of Rays | Method of Measur'g | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Platinum | Platinum to Water |
|---|---|---|---|---|---|
| | 0 | 12.4 | | | |
| | Water | 37.2 | | | |
| | 0 | 12.4 | | | |
| | Platinum | 23.0 | 67% | 46.3% | 0.69 |
| | 0 | 12.4 | with | with | with |
| | Water | 37.8 | correction | correction | correction |
| Unfiltered | 0 | 12.2 | for the | for the | 0.70 |
| X-rays | Platinum | 23.0 | insulation | insulation | |
| | 0 | 12.4 | error | error | |
| | Water | 38.0 | 76.6% | 53.3% | |
| | 0 | 12.6 | | | |
| | Platinum | 23.4 | | | |
| | 0 | 12.4 | | | |

| Hardness of Rays | Method of Measur'g | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Platinum | Platinum to Water |
|---|---|---|---|---|---|
| | 0 | 12.2 | | | |
| | Water | 30.0 | | | |
| | 0 | 11.4 | | | |
| | Platinum | 17.4 | 60.0% | 28.5% | 0.48 |
| | 0 | 12.0 | with | with | with |
| X-rays filtered | Water | 29.4 | correction | correction | correction |
| with 3 mm. | 0 | 11.8 | for the | for the | 0.47 |
| aluminum | Platinum | 16.8 | insulation | insulation | |
| | 0 | 11.6 | error | error | |
| | Water | 28.4 | 70% | 33% | |
| | 0 | 11.6 | | | |
| | Platinum | 15.4 | | | |
| | 0 | 11.0 | | | |
| | 0 | 13.2 | | | |
| | Water | 27.6 | | | |
| | 0 | 13.2 | | | |
| | Platinum | 16.2 | 52.2% | 19.0% | 0.36 |
| | 0 | 13.2 | with | with | with |
| X-rays filtered | Water | 27.4 | correction | correction | correction |
| with 10 mm. | 0 | 13.2 | for the | for the | 0.37 |
| aluminum | Platinum | 16.2 | insulation | insulation | |
| | 0 | 12.8 | error | error | |
| | Water | 27.8 | 59% | 22% | |
| | 0 | 13.0 | | | |
| | Platinum | 16.4 | | | |
| | 0 | 13.2 | | | |
| | 0 | 11.8 | | | |
| | Water | 22.8 | | | |
| | 0 | 11.4 | | | |
| | Platinum | 13.2 | 50.0% | 13.5% | 0.27 |
| | 0 | 11.6 | with | with | with |
| X-rays filtered | Water | 22.6 | correction | correction | correction |
| with 1 mm. | 0 | 11.2 | for the | for the | 0.27 |
| copper | Platinum | 13.4 | insulation | insulation | |
| | 0 | 11.4 | error | error | |
| | Water | 23.2 | 56.5% | 15.5% | |
| | 0 | 12.0 | | | |
| | Platinum | 13.4 | | | |
| | 0 | 11.4 | | | |
| | 0 | 21.4 21.0 21.4 | | | |
| | Water | 25.6 25.6 26.2 | | | |
| Gamma-rays | 0 | 21.2 21.4 21.4 | 17.3% | very small | very small |
| | Platinum | 21.4 21.2 21.6 | | | |
| | 0 | 21.2 21.4 21.4 | | | |

We see from this table that here also marked differences are present in the ratio of the degree of absorption in water and in platinum.

*Comparison of Absorption in Water and in Selenium.*

The reacting body in the Fürstenau intensimeter is chiefly selenium. To obtain an idea of the degree of error of this test body we determined the absorption of water and selenium with

the various hardnesses of rays. We compared the absorption in 5 cm. of water with that in selenium of a thickness of 1.5 mm. The results are contained in the following table.

COMPARISON OF ABSORPTION OF X- AND GAMMA-RAYS IN WATER AND SELENIUM

| Hardness of Rays | Method of Measur'g | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Selenium | Selenium to Water |
|---|---|---|---|---|---|
| | 0 | 10.6 | | | |
| | Water | 33.2 | | | |
| | 0 | 10.6 | | | |
| | Selenium | 51.0 | | | |
| | 0 | 10.8 | 68.0% | 79.0% | 1.16 |
| | Water | 34.0 | with | with | with |
| | 0 | 10.8 | correction | correction | correction |
| Unfiltered | Selenium | 52.0 | for the | for the | 1.14 |
| X-rays | 0 | 10.6 | insulation | insulation | |
| | Water | 34.8 | error | error | |
| | 0 | 11.2 | 78.2% | 89.6% | |
| | Selenium | 54.0 | | | |
| | 0 | 11.2 | | | |
| | Water | 34.8 | | | |
| | 0 | 11.2 | | | |
| | 0 | 12.2 | | | |
| | Water | 24.8 | | | |
| | 0 | 12.2 | | | |
| | Selenium | 32.4 | | | |
| | 0 | 11.8 | 51.0% | 63.4% | 1.24 |
| | Water | 23.6 | with | with | with |
| X-rays filtered | 0 | 11.8 | correction | correction | correction |
| with 3 mm. | Selenium | 33.2 | for the | for the | 1.23 |
| aluminum | 0 | 12.0 | insulation | insulation | |
| | Water | 24.0 | error | error | |
| | 0 | 12.0 | 59.4% | 73.0% | |
| | Selenium | 32.8 | | | |
| | 0 | 12.0 | | | |
| | Water | 25.4 | | | |
| | 0 | 12.0 | | | |
| | 0 | 11.4 | | | |
| | Water | 28.2 | | | |
| | 0 | 11.6 | | | |
| | Selenium | 44.8 | | | |
| | 0 | 11.4 | | | |
| | Water | 28.0 | | | |
| X-rays filtered | 0 | 11.6 | | | |
| with 10 mm. | Selenium | 44.2 | 59.3% | 74% | 1.25 |
| aluminum | 0 | 12.0 | | | |
| | Water | 28.6 | | | |
| | 0 | 11.2 | | | |
| | Selenium | 44.4 | | | |
| | 0 | 11.6 | | | |
| | Water | 28.6 | | | |
| | 0 | 11.6 | | | |

| Hardness of Rays | Method of Measur'g | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Selenium | Selenium to Water |
|---|---|---|---|---|---|
| | 0 | 10.6 | | | |
| | Water | 20.2 | | | |
| | 0 | 11.0 | | | |
| | Selenium | 20.4 | | | |
| | 0 | 10.8 | 46.8% | 47.1% | 1.00 |
| | Water | 20.6 | with | with | |
| | 0 | 10.6 | correction | correction | |
| X-rays filtered | Selenium | 20.8 | for the | for the | |
| with 1 mm. cu. | 0 | 10.6 | insulation | insulation | |
| | Water | 20.2 | error | error | |
| | 0 | 11.0 | 54.8% | 54.8 | |
| | Selenium | 20.6 | | | |
| | 0 | 10.8 | | | |
| | Water | 21.0 | | | |
| | 0 | 11.0 | | | |
| | 0 | 21.4 21.4 21.6 | | | |
| | Water | 27.8 27.8 27.0 | | | |
| Gamma-rays | 0 | 21.6 21.8 21.6 | 22.4% | 2.5% | 0.11 |
| | Selen'm | 22.4 22.2 22.2 | | | |
| | 0 | 21.6 21.8 21.6 | | | |

We see from this table that marked differences also exist in the ratios of the degree of absorption in water and in selenium with the different hardnesses of rays. However, the differences, when employing X-rays, are not as well marked as with silver and platinum. Quite considerable differences also exist in this instance between the hardest X-rays and gamma-rays.

*Comparison of Absorption in Air and in Water.*

The air in the ionization chamber serves as the reagent in the dosimeters based on the ionization method.

The great transmissibility of air toward X-rays made it necessary to modify the method of experimentation with which the measurements of absorption had been performed as described in the preceding paragraphs. In order to obtain approximately exact measuring results layers of air of a thickness of several meters were necessary as absorbing bodies, especially when using hard rays.

The exact method of experimentation, as schemetically reproduced in Fig. 15 is as follows: A narrow beam of X-rays which was cut out from the X-rays emitted from the focus of a Coolidge tube by the diaphragms $B_1$ and $B_2$ struck the ionization chamber of the measuring instrument described on page 10. The ionization chamber was placed at a distance of 6 meters from the focus. A layer of air of a thickness of 5 meters respective to a layer of water 1 cm. thick could be interposed in the following manner: Two iron pipes of a diameter of 15 cm. and a length of 5 meters were mounted upon a

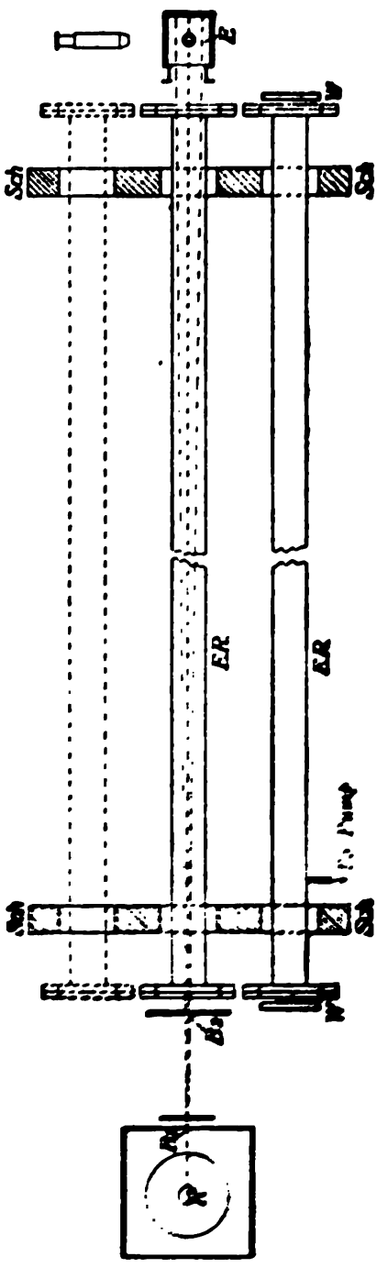


Fig. 15.

large wooden table. The ends of these pipes were closed with sheets of celluloid 1 mm. thick and mounted flanges which were packed with sealing wax. One of these pipes was connected to a Goede capsule pump and could be evacuated to a few millimeters of air pressure, while in the other pipe the air could be compressed by means of a tire pump and a tire valve. A pressure of one atmosphere could be obtained as read from a manometer. A wooden sled, on which both pipes were mounted enabled one to bring either the pipe filled with air or the one evacuated from air into the course of the rays. The layer of water W, which was to be tested was contained in a celluloid box of 1 mm. wall thickness. It could be inserted in the radiation beam at the end turned toward the tube as well as at the end turned away from the tube. The mean was taken from the absorption measurements with both positions of the layer of water. Pains were taken in the selection of the radiation beam, that the latter did nowhere strike the walls of the iron pipe and penetrated nothing else but the celluloid cover plates. The latter and also the celluloid box serving to hold the water were of the same thickness so that a source of error could not arise therefrom. The course of the measuring conformed to those described in the preceding experiments.

COMPARISON OF ABSORPTION OF X- AND GAMMA-RAYS IN WATER AND AIR

| Hardness of Rays | Method of Measuring | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Air | Air to Water |
|---|---|---|---|---|---|
| | Without air | 22.6 | | | |
| | With water St. 1 | 33.8 | | | |
| | Without air | 22.4 | | | |
| Unfiltered | With water St. 1 | 32.4 | 32.5% | | |
| X-rays | Without air | 22.4 | | | |
| | With water St. 1 | 34.0 | | | |
| | Without air | 22.6 | | | |
| | Without air | 22.0 | | | |
| | With air | 30.2 | | | |
| | Without air | 22.4 | | | |
| " | With air | 30.4 | | 27% | |
| | Without air | 22.8 | | | |
| | With air | 31.2 | | | |
| | Without air | 21.8 | | | |
| | Without air | 22.6 | | | |
| | With water St. 2 | 36.4 | | | |
| | Without air | 22.6 | | | |
| " | With water St. 2 | 36.2 | 38% | | 0.76 |
| | Without air | 22.4 | | | |
| | With water St. 2 | 37.0 | | | |
| | Without air | 21.8 | | | |

| Hardness of Rays | Method of Measuring | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Air | Air to Water |
|---|---|---|---|---|---|
| | Without air | 34.0 | | | |
| | With water St. 1 | 44.2 | | | |
| X-rays filtered | Without air | 33.8 | | | |
| with 3 mm. | With water St. 1 | 44.0 | 20.8% | | |
| Aluminum | Without air | 34.0 | | | |
| | With water St. 1 | 44.8 | | | |
| | Without air | 34.4 | | | |
| | Without air | 34.4 | | | |
| | With air | 40.8 | | | |
| | Without air | 34.6 | | | |
| " | With air | 42.7 | | 20% | |
| | Without air | 34.2 | | | |
| | With air | 41.0 | | | |
| | Without air | 34.8 | | | |
| | Without air | 35.0 | | | |
| | With water St. 2 | 47.6 | | | |
| | Without air | 35.2 | | | |
| " | With water St. 2 | 46.0 | 25.2% | | 0.74 |
| | Without air | 34.2 | | | |
| | With water St. 2 | 46.2 | | | |
| | Without air | 35.0 | | | |
| | Without air | 44.0 | | | |
| | With water St. 1 | 51.8 | | | |
| X-rays filtered | Without air | 42.0 | | | |
| with 10 mm. | With water St. 1 | 50.6 | 13.5% | | |
| Aluminum | Without air | 44.6 | | | |
| | With water St. 1 | 53.6 | | | |
| | Without air | 46.2 | | | |
| | Without air | 46.0 | | | |
| | With air | 52.2 | | | |
| | Without air | 44.2 | | | |
| " | With air | 51.3 | | 13.5% | |
| | Without air | 45.4 | | | |
| | With air | 54.2 | | | |
| | Without air | 47.0 | | | |
| | Without air | 46.0 | | | |
| | With water St. 2 | 56.4 | | | |
| | Without air | 45.0 | | | |
| " | With water St. 2 | 56.4 | 18.0% | | 0.78 |
| | Without air | 46.6 | | | |
| | With water St. 2 | 57.3 | | | |
| | Without air | 47.8 | | | |
| | Without air | 62.0 | | | |
| | With water St. 1 | 74.2 | | | |
| X-rays | Without air | 64.0 | | | |
| filtered with | With water St. 1 | 72.6 | 13% | | |
| 1 mm. cu. | Without air | 61.5 | | | |
| | With water St. 1 | 73.0 | | | |
| | Without air | 63.8 | | | |

| Hardness of Rays | Method of Measuring | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Air | Air to Water |
|---|---|---|---|---|---|
| | Without air | 64.2 | | | |
| | With air | 73.6 | | | |
| | Without air | 62.4 | | | |
| X-rays filtered | With air | 71.4 | | 12% | |
| with 1 mm. cu. | Without air | 62.0 | | | |
| | With air | 71.4 | | | |
| | Without air | 65.0 | | | |
| | Without air | 64.0 | | | |
| | With water St. 2 | 75.7 | | | |
| | Without air | 62.2 | | | |
| " | With water St. 2 | 73.6 | 16% | | 0.80 |
| | Without air | 60.0 | | | |
| | With water St. 2 | 74.4 | | | |
| | Without air | 63.2 | | | |

*The table proves that the differences in the degree of absorption in water and in air of rays of different hardnesses deviate so little from each other, that they may be neglected.*

It would have been desirable to also carry out the comparison of absorption of gamma-rays in air and in water. Difficulties, however, immediately arise in such comparative measurements caused by the great penetration power of the gamma-rays as well as by the impossibility to guard against undesirable radiations. We originally had the intention to carry out the comparative measurements according to a different method in which air would be employed in the liquid state. However, we had to postpone the measurements, as it was impossible on account of war times to obtain the necessary quantities of liquid air.

*If we sum up the results of the experiments described we see that of all the test substances considered, air alone answers all the requirements which, from a theoretical standpoint, were placed on a test body as mentioned at the beginning of this chapter.*

The ratio of the degrees of absorption in water and in the test bodies is only constant in water and air for the different hardnesses of rays.

We proved this by experimentation with the different hardnesses of Röntgen-rays only in air. We were obliged to postpone the direct experimental proof of the constancy of the ratio of the degrees of absorption in air and water for gamma-rays. The probabilities are that the ratio for gamma-rays is the same as that for X-rays. The air, like the biologic object, is composed of bodies of low atomic weight. If we did prove a constancy for the ratio of the degrees of absorption in the biologic object and water we must assume that the ratio in water and air will be also constant for hard gamma-rays. A dependence of the size of the ratio of the degrees of absorption in water and in the test objects on the

hardness of the rays is only then observed if test substances of such atomic weights are used that lie within the characteristic range of the hardness of these X-rays.

Accordingly only those dosimeters are to be recommended which use air as test body for comparative measurements of the dose with the different hardnesses of rays.

The other dosimeters may be employed in the comparative measurements of the dose obtained with one and the same quality of radiation. As we possess in this instance a definite ratio of the degree of absorption in the test body and in the biologic object, the degree of the reaction in the test body is proportional to the dose in the biologic object.

The differences in the ratios between the values of absorption in water and the other test bodies may be traced back to selective absorption. This selective absorption as source of error has been frequently discussed in the literature. Attention has been especially drawn to the so-called silver error of the Kienböck strips. It has been claimed that, with a known hardness of rays, the Kienböck strips as dosimeter would indicate a dose many times below as well as above this range of hardness. This statement has never been directly proven by experimentation. One, however, felt justified to maintain this opinion through the investigations of Barkla, Adler and others on the selective absorption of X-rays in different bodies. These investigators observed a sudden increase in the absorption to multiple degrees with a slight increase in the hardness of rays as soon as one entered the range of the characteristic radiations of the metals.

Barkla and his students did not use in their experiments the primary rays from an X-ray tube to produce variations in the hardness of the rays. They employed the so-called homogeneous secondary rays or fluorescent radiations arising from substances of various atomic weights to investigate the absorption in certain substances. The range of hardness of these secondary rays is a limited one, as the name homogeneous radiation already implies, and the hardness is absolutely dependent on the atomic weight of the secondary radiator.

The well-marked limits and the predominence of the domain of the selective absorption of a body in the experiments of Barkla are due to the employment of these homogeneous radiations.

The range of hardness, respectively the range of wave-lengths, of the primary X-rays is a wide one even if they are filtered. A large portion of the rays striking the body surface are of little importance in selective absorption. The domain of selective absorption will not be so sharply marked with primary radiations as with homogeneous secondary rays and the domain of selective absorption will be more or less obliterated. The selective absorption will be the less marked the smaller the range of the wave-length is

which pertains to the selective absorption, in comparison to the range of the wave-length of the total radiation.

The domain of selective absorption of the test bodies considered above is confined to rather soft rays with the exception of platinum as has been demonstrated by special recent investigations with the spectral analytical methods. The hardness of rays employed in our experiments are for the most part beyond the maximum for those of selective absorption and are removed the farther from it the stronger we filter.

If we consider the results of the measurements of comparative absorption in water and test bodies from this viewpoint, we observe that an especially strong absorption does not appear in any of our test bodies with the hard rays employed, as for instance, has been claimed for the so-called silver error of the Kienböck strips. Only the difference in the ratio between the values of absorption in water on one hand, and in the test bodies silver, platinum and selenium on the other enables one to recognize the influence of selective absorption.

*Investigations on the Degree of Sensitiveness and Dependence of the Dosimeters which are based on the Test Objects examined in the preceding chapters.*

The efficiency of measurements is not only judged from the test bodies but also from the degree of sensitiveness and dependence of the method.

If we desire to examine a measuring method as to its sensitiveness and dependence a practical way would be to use a constant source of rays for the investigation. With a constant source of radiation we may, in a measurable manner, vary the dose respective to the intensity by changing the time respective to the distance and thus determine the sensitiveness. Further we may obtain a true picture of the dependence of the method by frequently repeating the measurements under like conditions.

The X-ray tube is not at all a source of constant radiations. The intensity and the composition of the rays depend on many factors, such as the construction of the inductor or transformer, the manner of operation, the condition of the tube, etc., also on factors that may change during the operation which are beyond our control.

On the other hand, radio-active substances, especially radium and mesothorium, furnish a radiation, the intensity and composition of which are solely characterized by the radio-active substances as such and by their amount. The radiation may be considered as constant due to the great length of life of radium and mesothorium and therefore may be used to test the dosimeter as to sensitiveness and dependence. To perform the standardization with a single preparation even with the strongest found in our possession, namely 70 mg. radium element activity, was im-

possible. The intensity of the radiation is already so minute at a comparatively short focal distance that the times of discharge would be so long that the sources of error previously discussed would play a predominant rôle. We possessed a large amount of

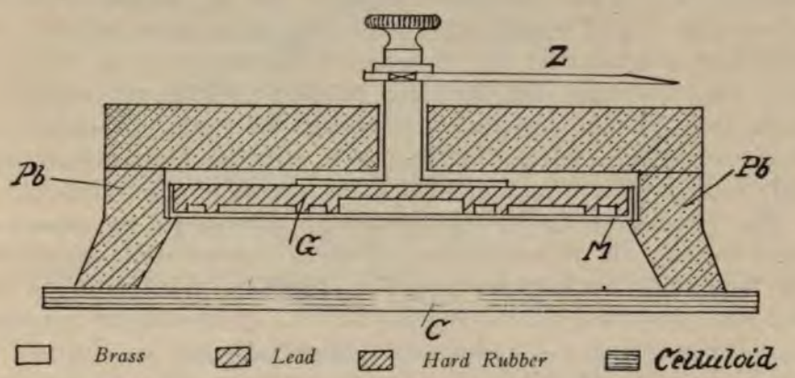


FIG. 16.

radium and mesothorium of more than 1 g. radio-activity in 23 preparations partly in a cylindrical and partly in a flat capsular form. They were placed in a radiation apparatus shown schematically in Fig. 16 and photographically in Fig. 17. To obtain

FIG. 17.

a radiation field useful for our measurements we constructed the carrier as follows:

A closely fitting hard rubber disk G was placed within a flat brass box M of a wall thickness of 1.5 mm., of a diameter of 15 cm. and of a height of 1 cm. Furrows were cut in the hard rubber plate of such form, size and location, that all the preparations could be distributed almost evenly upon the plate (see Fig. 17).

The brass box, which also served as a filter was inserted in a

round lead chamber Pb of a wall thickness of 2 cm. The lower open surface exposed to the object to be radiated was closed by a celluloid plate C of 5 cm. thickness. It extended 3 cm. beyond the periphery of the lead chamber to render harmless the secondary radiation arising in the lead chamber. As the preparations of radium and mesothorium varied considerably in their activity, the possibility existed that the regions of the object to be radiated lying directly under the stronger preparations, might receive a larger dose than the regions lying beneath the weaker preparations. To overcome this defect, the filter box with the preparations was made to turn around an axis during the course of the radiation.

The velocity of the rotation could be determined by means of a dial on the scale placed on the surface of the radiation apparatus. The time intervals between single rotations were adjusted to the total time consumed during the radiations. A mechanical arrangement for rotating the radium carrier could also be attached if radiations of short durations were to be given, thus to insure a steady rotation of the filter and radio-active preparations. The distance of the radio-active preparations from the lower surface of the celluloid plate could be varied at will by the interposition of lead rings. The distance usually amounted to 4 cm. We chose the distribution of the radio-active substance on such a large surface for the reason that with this method of distribution the decrease of intensity with the distance from the radiation source does not any more obey the law of squares but shows a gradual decrease of intensity which was very desirable for our purposes of radiation of biologic objects.

Through a series of experiments a distribution of the preparations was found that gave the most homogeneous radiation field. To determine the homogeneity of the radiation field we made use of the apparatus for measuring the intensity of rays described on page 9. The ionization chamber of the instrument could, by the use of a stand, be brought to any desired and measurable position in relation to the radiation apparatus, which we will call the "radium cannon." The measuring was performed so that the time was observed within which the electrometer leaf passed through 5 divisions of the scale. In this manner we determined the distribution of the intensity of the radiation parallel to the under surface of the filter at a distance of 2 cm. and the decrease of the intensity of the radiation in the centre of the ray beam with an increase in distance from the source of radiation.

The error of the undesirable radiation and so forth due to the considerably long duration of the time for a reading was always taken into account.

The results of the measurements are recorded in the two following tables. They are reproduced graphically. Fig. 18 shows the distribution of the intensity parallel to the lower surface of

the filter, and Fig. 19 represents the decrease of the radiation intensity with distance.

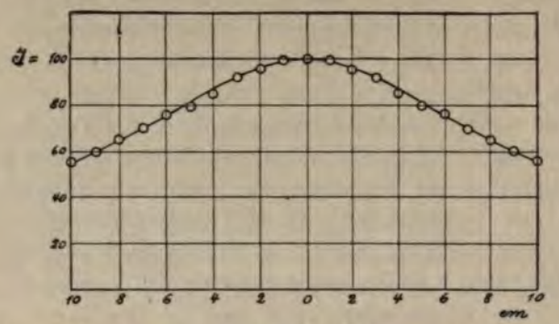


Fig. 18.—The distribution of the intensity of the gamma-rays of the radium cannon parallel to the base at a distance of 2 cm.

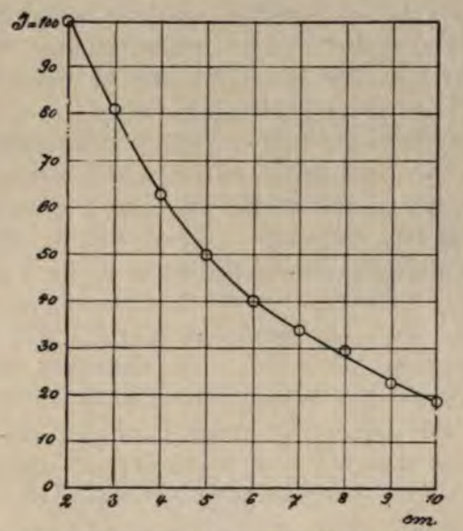


Fig. 19.—Distribution of the intensity of the gamma-rays of the radium cannon vertical to the base.

We conclude from the graphs that we did not attain a perfectly even distribution of the intensity with the radiation beam employed, but the intensity of the rays within a space of the size of a few ccm. varies so little that comparative measurements could be made within this space with some exactness.

### *Investigations on the Dependence and Sensitiveness of the Iontoquantimeter*

We designated the measuring method, which uses air as a test body, as the one most free from any objection. Such dosimeters have been recently placed on the market. We mention the iontoquantimeter of Reiniger, Gebbert and Schall and the ionometer of Siemens and Halske. We had at our disposition a dosimeter of

Reiniger, Gebbert and Schall. It consists of an electrometer which is connected to an ionization chamber with a cable well protected against radiations. The ionization chamber is exposed to the rays to be measured. The discharge of the electrometer caused by the ionization of air in the ionization chamber serves as a measure for the dose applied.

As simple as the method appears to be, it harbors the most varied sources of errors which may interfere with dependence.

Insulation: One of the sources of errors is found in the insulation of the electrometer system. If the insulation of the system is not satisfactory, a discharge of the system will occur without the action of rays. Accordingly one might measure the dose as too small if the undesirable rays act at the same time on the ionization chamber. This source of error has been avoided as far as possible by the use of amber and tested rubber as insulation material. The insulation, however, must be tested before and after each use, as disturbances in the insulation may occur during an extended use through dust, humidity and so forth.

*Dielectric Polarization.*—Another source of error also found in the insulation material is the dielectric polarization of the latter which usually has been disregarded. The charge of the electrometer system creeps with time slowly into the insulation material, until it is completely polarized. This part of the charge again leaks out from the dielectric at the time of discharge of the electrometer system. Therefore, if one intends to determine the dose with a dosimeter that has not been charged for some time, the dose will be measured too small. The influence of this source of error is the greater the longer the time lasts within which the desired dose is obtained. On the other hand, if the dosimeter had been more or less in a state of charge for a longer time, that is, if the dielectricum has become polarized, then the source of error, when we measure the dose, will act in the opposite direction and the dose will be measured too large; for during the discharge a part of the electric current that previously crept into the dielectric will again leak out. This error also will be the greater the longer the time consumed to attain the desired dose.

In order to obtain an idea of the source of error we instituted a series of experiments in which we determined the amount of the quality of electricity which crept in and leaked out of the insulation within the time periods during which the applications had to be made. The quality of the insulation of the electrometer system naturally played an important rôle on these experiments.

In determining the quality creeping into the dielectric the amount will be measured too high, because part of the charge of the electrometer is lost at the same time due to defective insulation.

In determining the amount of electricity leaking out with the discharge, the defect in the insulation will act in the opposite

direction, and the quantity of electric current leaking out of the insulation is apparently decreased.

The following curves (see Fig. 20) represent the values in a series of experiments which were performed with one of the iontoquantimeters used by us.

Curve I was obtained so that the discharge of the electrometer of a freshly charged iontoquantimeter was observed every 5 minutes. The curve II was gained in an analogous manner. However, the iontoquantimeter in this case was kept for 5 hours in a completely charged state at the point O.

We see from the curves that a considerable difference exists between them. The freshly charged instrument has lost more than

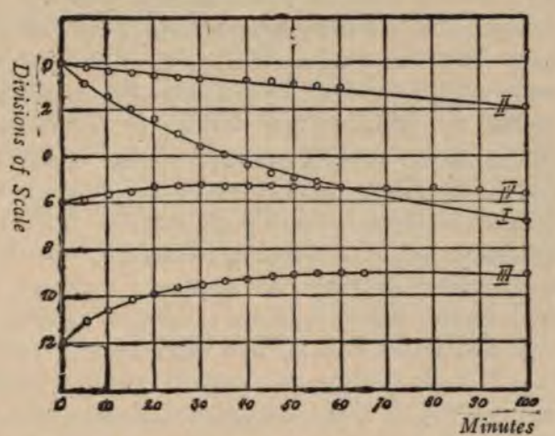


FIG. 20.—Errors of isolation and dielectricum of the iontoquantimeter.

one-half of the twelve divisions of the scale within a period of time of 100 minutes, while the iontoquantimeter, charged for several hours has not quite lost two divisions of the scale within the same time period. This graph did not materially change if the time period of charge was extended before the experiment. We, therefore, possess in graph II an approximate value for the size of the defect in the insulation.

The graph III reproduces the result of an experiment in which the iontoquantimeter was charged for 5 hours prior to the test; it then was discharged in the shortest time possible while the movement of the electrometer was observed every 5 minutes. The graph shows that the electrometer goes back through three divisions of the scale within a time duration of 100 minutes. The graph at first ascends steeply and after a time of about 50 minutes runs horizontally. The error in the dielectric and the defect of insulation are in equilibrium after this time.

These graphs naturally give us only a general idea of the propositions just discussed; the conditions in reality are different. The

sources of error may be considerably lessened in practical use by the observations made.

We will be able to prevent the error of creeping in of the charge by charging the electrometer for some time prior to its use. The error of creeping out is in reality much less, as expressed in graph III, for the discharge of the instrument during dosation does not take place suddenly as in graph III, but very slowly. We will arrive at a determination of the magnitude of this error much more closely, if, after keeping the instrument charged for a more or less long time, we do not discharge it to the end but rapidly to the middle of the scale which corresponds to a mean potential, and then observe the movement of the hand of the electrometer. Curve IV, which is a reproduction of the result of such an experiment, shows that, indeed, the movement of the hand of the electrometer is much slower. We observed a slight rise of not quite one division of the scale within the first 30 minutes, the hand then remains in the same position. The error of insulation in this instance acts most favorably by almost wholly compensating the error of creeping out of the charge from the dielectric. The error will be still smaller than determined in curve IV during the quite gradual discharge taking place while performing dosation, and in reality it will not materially rise above 5 per cent.

*Electrostatic Protection.*—It is especially necessary to observe a good electrostatic protection of the electrometer system during the operation of X-ray tubes on account of the strong electric oscillations in the room. The iontoquantimeter has been quite extensively protected in this regard. However, it is deemed advisable to perform a few controls to guard against such sources of error.

*Undesirable Radiation.*—The rays to be measured must alone enter the ionization chamber and here only cause the discharge of the electrometer during the measuring of the dose with the iontoquantimeter. A discharge caused by the entrance of rays in the cable or in the case of the electrometer would cause a source of grave error under certain circumstances. The electrometer housing of the iontoquantimeter is protected from X-rays by a thick layer of lead. A heavy metallic protection of the cable against X-rays has not been made. However, a disturbing ionization in it need not be feared as the conducting wire is everywhere enclosed with the best insulation material. The attachment of the wire to the ionization chamber is also rendered tight by paraffin filling, so here also a disturbing ionization cannot occur. The absence of air in all parts of the conductor of the iontoquantimeter is a decided advantage in comparison to other instruments in which the conducting wire is supported by insulation rings within the metallic tube filled with air. The above-mentioned defects of the dielectric are almost entirely absent from this kind of conductor. However,

the error of undesirable radiations may become considerably larger in conductors filled with air, especially with hard rays, than the defects of the dielectric.

It goes without saying that we tested the iontoquantimeter for undesirable radiations in spite of these considerations. For this purpose the ionization chamber was protected all around with a thick sheet of lead, through which X-rays could not penetrate. The ionization chamber thus protected was exposed to the rays of a roentgen tube and placed in a position usually maintained during the measurements of the dose. The time-duration of the action of the X-rays conformed to the time which suffices for the administration of the usual dose. A series of such tests revealed that the undesirable radiation, when using the X-rays, was so small in the iontoquantimeter employed by us that it could be neglected when using this instrument as a dosimeter.

The conditions are quite different when gamma-rays of radium or mesothorium are used. Undesirable rays do not act as disturbing factors in the cable. However, the lead-wall of the electrometer box does not afford protection against the entrance of these penetrating rays. A considerable reinforcement of the lead-wall also would not afford protection. As the size of the space of the ionization chamber is much smaller than the air space of the electrometer case, the error caused by the entrance of undesirable rays into the electrometer case is very important in spite of the much greater distance of the electrometer case from the radiation source, and it must be taken into account. Therefore the size of this error must be measured with each determination of a dose of gamma-rays.

An example will easily explain the method of the determination of the undesirable radiation.

We intend to apply a dose at a certain place of a biologic object which corresponds to five complete discharges of the scale of the iontoquantimeter. The source of radiation remains in the same position as the ionization chamber during the entire time.

The time during which a complete discharge of the scale occurs amounts to 10 minutes. Now let us remove the ionization chamber, while the radiation source remains in the same location, and place the chamber directly beside the electrometer box and, after charging the electrometer system, again observe the movement of the electrometer during 10 minutes. We observe that the hand of the electrometer passes through 5 divisions of the scale within 10 minutes. This amount does not wholly equal the size of the undesirable radiation, but it approaches it very closely, for one not only measures the undesirable radiation but also the radiation in the ionization chamber. But, as mentioned, the air volume in the ionization chamber is disproportionately much smaller than the air volume in the electrometer casing. The ionization activated in the

air volume of the ionization chamber may be neglected as both air spaces are now located at an equal distance from the source of radiation.

During the ten minutes in which the rays acted on the ionization chamber and the hand of the electrometer passed through the entire scale, only ⅘ of the discharge was caused by the desirable and ⅕ by the undesirable radiation. If we intend to apply a dose which corresponds to 5 consecutive discharges of the entire scale of the electrometer, we must not ray 5 times 10 minutes but 5 times 12 minutes, as a constant source of error is present when using radium-rays.

A similar correction must be made in all cases in which gamma-rays of radium or mesothorium are used.

*Errors of construction of the ionization chamber.* The sources of error so far discussed were founded in the method as such and were, as we saw, partly unavoidable.

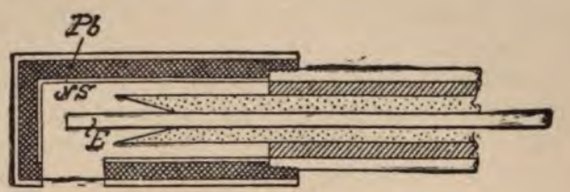


FIG. 21.

Another source of error may be added, found in the iontoquantimeter obtainable in the market. The error is due to the faulty construction of the ionization chamber.

The ionization chamber of the iontoquantimeters found in the market consists of a square foursided closed brass tube of a square transverse section, of a clear length of 37 mm., a clear height of 10 mm., and a clear width of 10 mm. and a wall thickness of 4.5 mm. (See Fig. 21.) The brass tube is lined on the interior with a sheet of lead of a thickness of 3 mm., and this again with a thin sheet of German silver of 1 mm. thickness. The latter, probably, serves the purpose of giving the interior space a more stable form than could be had with the easily compressable lead. The square transverse section of the interior space is of a volume of 1 sq. cm. A small square window F of 1 sq. cm. is located on the upper surface of the chamber. The latter is closed by a thin leaf of aluminum. The rays to be measured are supposed to enter the chamber through the window. A brass rod E of 2 mm. diameter and a length of about 1 cm. serves as the inner electrode. It is insulated with amber.

The air space of the volume 1 ccm. serves for the measuring. The volume is fixed by the aluminum window. The walls of the

chamber are supposed to be heavy enough to keep undesirable radiations away from the air contained in the chamber, the size of which is quite large, as may be seen from Fig. 21.

The walls of the ionization chamber offer an adequate protection against X-rays, even against the relatively hard rays employed in our investigations. However, they cannot sufficiently check the hard gamma-rays of radium and mesothorium. Part of the penetrating rays will enter the ionization chamber through the brass and lead wall and thus contribute to the discharge of the electrometer. We will consequently read too large a dose on the instrument.

Another grave error of construction of the ionization chamber lies in the selection of the material. We approved the iontoquantimeter as preferable to all other dosimeters because we consider air as the least objectionable test object. If rays enter the interior of the ionization chamber just described through the aluminum window, the air in the chamber will become ionized and at the same time they activate secondary rays in the metal wall of the chamber, corpuscular secondary rays, secondary cathode rays, and also secondary rays of the character of the X-rays, and the scattered radiation. It is self-evident that these rays also will ionize the air within the chamber and are a source of error. The reason that these secondary rays may become an error can be explained as follows:

The hardness of the secondary radiation is proportional to the absorbed X-ray energy in the body from which the secondary rays are emitted. The hardness of the secondary rays will therefore obey similar laws as the absorption of the X-rays. As the walls of the ionization chamber consist of a metal of high atomic weight, the amount of ionization caused by the secondary rays will differ just as the ionization caused by X-rays in air will differ accordingly as qualities of rays of various hardnesses are measured.

The size of the error depends on the difference between the ionization of the secondary rays and the ionization of the X-rays. The proportion of ionization by secondary rays to that of ionization of X-rays of the air in an ionization chamber of such a small volume as used in the iontoquantimeter, is especially unfavorable because the primary rays are slightly and the secondary cathode rays arising in the walls of the chamber are strongly absorbed in the air volume. The error attributable to secondary rays may become so great that the ionization caused by the secondary rays will be many times greater than the ionization produced by the primary X-rays. The correctness of regarding the air as a test reagent in the iontoquantimeter may justly be doubted. It is possible, as we will see later, to construct an ionization chamber in which the wall radiation is completely removed and in which, therefore, air alone acts as the test body. Such a chamber is, however, unhandy

and so complicated in structure that it is unsuitable for practical dosimetry.

We may remove the error of the wall radiation by choosing in its construction conductive material of low atomic weight, for example, carbon or graphite, instead of the metals of high atomic weight found in the iontoquantimeter obtainable in the market. The wall radiation present in the chambers constructed of material of low atomic weight will not contribute to the source of error, because the secondary radiation from the carbon is proportional to the absorption of the primary radiation in carbon and therefore also proportional to the absorption in the biologic object. Though the low atomic weight of carbon renders this conclusion as probable we have, nevertheless, examined the absorption in carbon and water in an analogous manner as in the investigations of the test bodies employed in the ordinary dosimeters. We used for these measurements a plate of chemically pure carbon of a thickness of 4 cm. and the customary layer of water of a thickness of 5 cm.

In the following table the results of these measurements have been compiled.

COMPARISON OF ABSORPTION OF X- AND GAMMA-RAYS IN WATER AND CARBON

| Hardness of Rays | Method of Measuring | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Carbon | Carbon to Water |
|---|---|---|---|---|---|
| Unfiltered X-rays | 0 | 10.2 | 69% with correction for insulation error 78% | 62.3% with correction for insulation error 69.5% | 0.90 with correction 0.89 |
| | Water | 33.0 | | | |
| | 0 | 10.4 | | | |
| | Carbon | 28.4 | | | |
| | 0 | 10.2 | | | |
| | Water | 33.6 | | | |
| | 0 | 10.4 | | | |
| | Carbon | 27.4 | | | |
| | 0 | 10.4 | | | |
| | Water | 34.0 | | | |
| | 0 | 10.2 | | | |
| | Carbon | 28.0 | | | |
| | 0 | 10.6 | | | |
| | Water | 33.2 | | | |
| | 0 | 10.6 | | | |
| X-rays filtered with 3 mm. Aluminum | 0 | 11.6 | 50.8% with correction for insulation error 58% | 45.4% with correction for insulation error 51.7% | 0.90 with correction 0.89 |
| | Water | 22.6 | | | |
| | 0 | 11.6 | | | |
| | Carbon | 20.2 | | | |
| | 0 | 11.4 | | | |
| | Water | 23.2 | | | |
| | 0 | 11.2 | | | |
| | Carbon | 21.2 | | | |
| | 0 | 11.8 | | | |
| | Water | 23.8 | | | |
| | 0 | 11.8 | | | |
| | Carbon | 21.8 | | | |
| | 0 | 12.2 | | | |
| | Water | 24.8 | | | |
| | 0 | 12.2 | | | |

| Hardness of Rays | Method of Measuring | 5 Units of Scale of Electrometer in seconds | Absorption in Water | Absorption in Carbon | Carbon to Water |
|---|---|---|---|---|---|
| | 0 | 12.0 | | | |
| | Water | 26.6 | | | |
| | 0 | 12.0 | | | |
| | Carbon | 23.0 | | | |
| | 0 | 11.2 | | | |
| | Water | 27.2 | | | |
| X-rays filtered | 0 | 11.2 | | | |
| with 10 mm. | Carbon | 23.0 | 57.4% | 49% | 0.86 |
| Aluminum | 0 | 11.6 | | | |
| | Water | 27.2 | | | |
| | 0 | 11.4 | | | |
| | Carbon | 22.4 | | | |
| | 0 | 11.4 | | | |
| | Water | 28.2 | | | |
| | 0 | 11.6 | | | |
| | 0 | 10.4 | | | |
| | Water | 20.4 | | | |
| | 0 | 10.6 | | | |
| | Carbon | 17.0 | | | |
| | 0 | 10.2 | 47.0% | 38.5% | 0.80 |
| | Water | 19.8 | with | with | with |
| X-rays filtered | 0 | 10.6 | correction | correction | correction |
| with | Carbon | 17.0 | for | for | 0.81 |
| 1 mm. cu. | 0 | 10.2 | insulation | insulation | |
| | Water | 19.6 | error | error | |
| | 0 | 10.8 | 52.8% | 42% | |
| | Carbon | 17.4 | | | |
| | 0 | 10.6 | | | |
| | Water | 20.2 | | | |
| | 0 | 11.0 | | | |
| | 0 | 21.4 21.4 21.6 | | | |
| | Water | 27.8 27.8 28.0 | | | |
| Gamma-rays | 0 | 21.6 21.8 21.6 | 22.4% | 26.8% | 0.84 |
| | Carbon | 26.2 26.0 25.4 | | | |
| | 0 | 21.4 21.6 21.6 | | | |

We see from this table that the ratio of absorptions in carbon and water with the different hardnesses of rays may, indeed, be considered as constant for our purposes. Though the air in such an ionization chamber with carbon walls does not serve as a test body in its proper sense, as the secondary rays formed in the wall of the chamber also partly contribute to the ionization, still all the requirements are fulfilled with such a chamber on account of the low atomic weight of the carbon.*

The ionization chamber with graphite electrodes and walls and

* Besides carbon, other substances of low atomic weight which might be suitable for the construction of ionization chambers and electrodes such as celluloid, cow's horn, wood fiber, and so forth, have been tested for their absorption of rays in comparison to that of water. The measurements of all these substances proved that a good constant of the ratio of absorption exists in them and water with various hardnesses of rays. The substances named are suitable for the construction of ionization chambers if they have been rendered conductive to electricity by proper treatment, for instance, graphitizing the surface.

their connection with the flexible conductor to the electrometer was constructed as follows: Fig. 22 shows the construction in a schematic outline. The end of the rubber cable K, which contained the conductor to the electrometer, was inserted into the brass tube R. The latter was soldered to the flexible outer metal protecting wall of the cable and clamped to it with a hard rubber screw ring. The ionization chamber J was fastened down with the screw cap U. The chamber was composed of buffalo horn and constructed of one piece. The thickness of the wall was about 0.8 mm. The inner surface of the chamber as also part of the external surface which projected above the screw cap were covered with graphite. The graphite was rubbed in firmly with a steel polishing rod to render the layer of graphite as even and to impermeate the horn as firmly as possible.

The inner side of the ionization chamber, thus rendered conductive, served also as one of the electrodes. The other electrode E consisted of a small stick of carbon, which was attached to the measuring rod M. A piece of amber B of a suitable form served as a support and a means of insulation of the measuring rod from the carbon electrode. Care was taken that the end of the brass rod did not enter the chamber. The other end of the brass rod was soldered to the insulated wire. This end of the cable was removed from the insulated wire without touching it with the fingers or dirty tools in order to maintain the best properties of insulation. The air space that remained between the amber piece and the end of the rubber cable within the brass tube, was tightly filled with paraffin through the two openings O that could be closed with a screw cap. The suitable dimensions of the ionization chamber were, diameter of 10 mm. and length of 20 mm. The graphite electrode was 2 mm. thick and 15 mm. long. All dosations, even when using various qualities of rays may be performed with a chamber thus constructed. We at first used in our biologic investigations an ionization chamber of aluminum walls and electrode as the proper construction of the cow's horn ionization chamber had not as yet been perfected. We could use the results obtained with the aluminum chamber dosimeter, as it otherwise possessed the same sensitiveness and dependability. We applied the corresponding corrections as soon as we had gauged the aluminum chamber with the graphite chamber.

The aluminum chambers were similarly constructed as the carbon chambers. In one of the models the wall of the chamber consisted of an aluminum tube with a conical point of a wall thickness of 2 mm. This model was especially used in measurements within the body cavity, where a greater stability of the chamber is required.

A second model also was used for surface measurements, in which the wall thickness was chosen especially thin. It amounted to

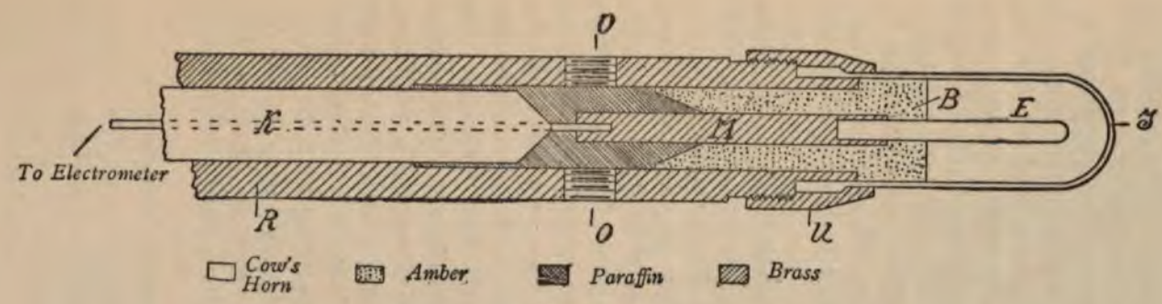


FIG. 22.

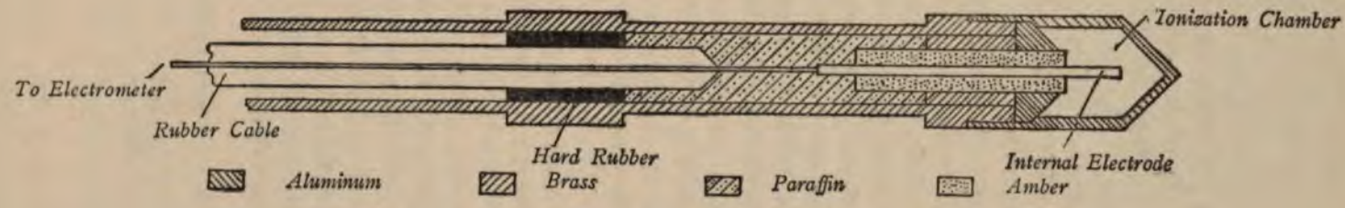


FIG. 23.

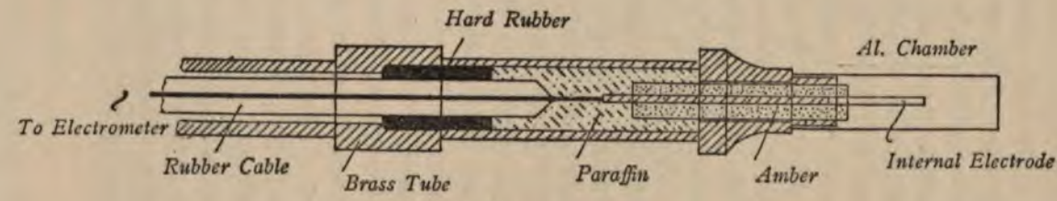


FIG. 24.

The charge on a monovalent ion in electrolysis = $4.77 \times 10^{-10}$ Electro Static Unit
mega megaion = $10^6 \times 10^6 \times 4.77 \times 10^{-10} = 477$ E.S.U.



of electricity which raises a sphere of a radius of 1 cm. to the unit of potential, i.e., 300 volts. According to Kohlrausch it is expressed with a small e. A unit also had been proposed by Szilard in describing his quantimeter. He proposed to express the dose in the number of ions which is produced in 1 ccm. of air under the influence of the rays to be measured. He declared as unit the *megamegaion.* We give preference to the electrostatic unit as unit of dose instead of the megamegaion, because the electrostatic unit is a known and absolute unit in the science of electricity and we do not deem it advisable to add a new unit to the innumerable units already existing.

We have minutely discussed the sources of errors, which are due to the construction of the iontoquantimeters found in the market. The scale, attached to Szilard's instrument, which expresses the dose in numbers of ions per ccm., is incorrect and requires a new gauging, which we have carried out. The following method for this procedure was decided on after a number of preliminary tests and appears to be free from any objections. In this the time is determined in which an electrometer system of a measurable capacity is discharged by a measurable potential through the ionization of a known volume of air in a chamber free from any defects of construction. This discharge time was compared with the discharge time of a constant radiation in the instrument to be standardized. The amount of electricity transported through ionization may be calculated from the known capacity of the standardized instrument and the loss of the potential measured. It can then be expressed in electrostatic units per ccm. of air if the volume of the ionization chamber is known.

### *The Arrangement of the Experiment*

*Ionization Chamber.*—It is a presupposition for the measuring of an ionization in a known volume of air respectively for the measuring of the quantity of electricity transported by the ionization in this volume of air, that the air be exclusively ionized by the X-rays and that a secondary radiation in the walls does not at the same time contribute to the ionization.

The principle of the ionization chamber used by us for the ionization and which possessed the presupposition of the absence of any wall radiation and yet permitted to determine the ionization in a measurable volume of air, was as follows:

The size of the beam of radiation is defined by adjustable diaphragms and enters the ionization chamber. The transverse section of the column of air in the ionization chamber ionized by the rays is determined by the diaphragm and by the known distance of the focus of the tube from the ionization chamber. The electrodes of the ionization chamber are placed parallel to the direction of rays so that they may not be struck by the rays. The

limits of the length of the ionized air column which should serve for the measuring are attained by placing before and behind the electrodes of the ionization chamber two accessary electrodes which are attached as close as possible to the proper electrodes. They produce an electrical accessary field which keeps all ions away from the proper electrodes that may arise externally to the ionized air columns defined by the position of the accessary electrodes. The ions produced by the wall radiation of the thin posterior wall of the ionization chamber and the diaphragms are thereby kept away from the measuring chamber proper. The volume of air in which the ionization is to be measured is determined by the diameter

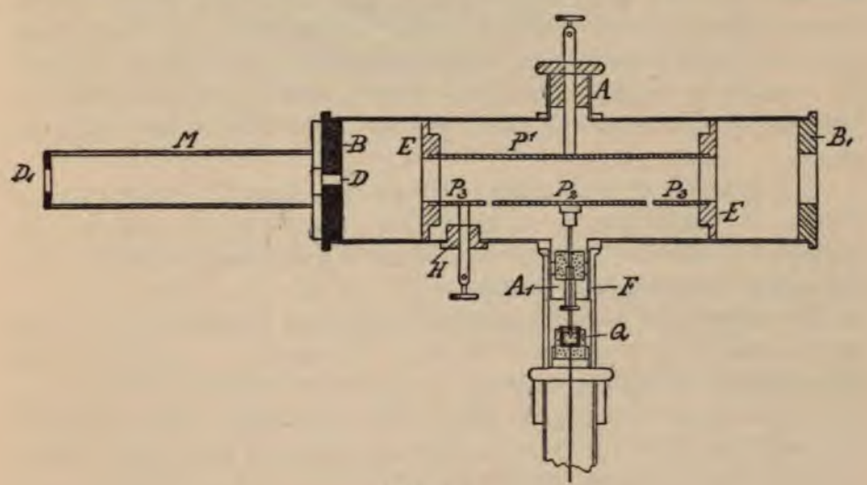


FIG. 25.

of the diaphragms and by the distance of both accessary fields. The ionization chamber used by us and based on this principle and reproduced in detail in Fig. 25, was constructed as follows:

Two plates of aluminum 1 mm. thick were placed in a round brass pipe 20 cm. long and 5 cm. in diameter. The upper plate $P_1$ which was grounded, was of a rectangular shape, 12 cm. long and 3.5 cm. broad. It was fixed parallel to the axis of the brass tube by a ring-shaped hard rubber support E. A brass stem with a binding post passed through an ebonite stopper to the exterior. The ebonite stopper was held in the adjoining tube. The lower plate $P_2$, which was to be connected to the electrometer, was also rectangular, 1.5 cm. wide and 6.5 cm. long. It was held parallel and at a distance of 2 cm. from plate $P_1$ by a copper rod which passed through a second adjoining tube A, exactly opposite to the first one. The copper-rod was insulated by amber. $P_2$ could be moved up and down by a locking screw. The plate $P_3$ served for the purpose of forming the accessary field in the interior of the brass tube. It surrounded the plate $P_2$ in the form of a rect-

angular rim and was kept at the same distance as $P_1$ from $P_2$ by the supports E. The space between $P_2$ and $P_3$ was designed as small as possible and was about 1 mm. wide. The connection of $P_2$ with the electric system was attained by a brass rod, which passed through the brass tube and was insulated with a hard rubber stopper and provided with a lockscrew. The side of the brass tube exposed to the source of radiation was closed by a lead disc B, 10 mm. thick, in which a circular opening 8 mm. wide was drilled centrally. It thus defined the radiation beam entering the ionization chamber. The opening was closed with a very thin plate of celluloid. The posterior cover $B_1$ was constructed of aluminum with a round opening of a diameter of 2 cm. which was closed with a very thin carbonized paper in order to obtain as few secondary rays as possible in the ionization chamber. It could be replaced by a small fluorescent screen of barium platinum cyanide for the purpose of correctly adjusting the apparatus within the radiation beam.

A brass tube M of a length of 12 cm. was inserted in the anterior cover. A diaphragm D of lead with an opening 10 mm. in size was placed at the outer end to prevent the entrance of undesirable rays into the ionization chamber.

The support of the ionization chamber was composed of a heavy brass tube of a diameter of 20 mm. It served at the same time the purpose of giving passage to the wire connecting the lower electrode $P_2$ of the electrometer. The connecting wire consisted of a fine polished copper wire, it ran coaxial and was kept isolated at the ends by amber supports. The wire terminated above in a small copper bowl Q which was amalgamated on the inside and contained mercury.

A piece of brass tubing F was attached to the upper end of the holder. It received the lower joint tube $A_1$ of the ionization chamber which fitted exactly into tube F. The amalgamated copper rod connected to the plate $P_2$ dipped into the bowl Q and thus effected a positive contact with the conducting wire of the electrometer.

The capacity of the air chamber is determined

1. By the size of the diaphragm, which limits the radiation beam;
2. By the distance of the electrodes from the accessary field;
3. By the divergence of the raybeam, which is dependent on the distance of the anticathode from the ionization chamber.

The diameter of the circular diaphragm is 8 mm.; the distance between the accessary electrodes 65 mm., and the distance of the source of radiation from the center of the measuring chamber 90 cm. The measuring chamber therefore has the form of an obtuse cone with a diameter of the end surfaces of 8.5 respectively 10 mm., and a height of 65 mm.

The volume of the obtuse cone is 4.38 ccm. according to the established calculations for obtuse cones.

*The Electrometer System.*—We used the instrument described on page 81 as electrometer system for measuring the intensity. In place of the ionization chamber used for the measuring of intensity we substituted the air chamber just described. It was connected to the electrometer with the proper connections.

*Measuring Condenser.*—For the determination of the capacity of the electrometer system we use the method of division of the potential. According to this method the electrometer system, the capacity of which one intends to determine, is charged to a known potential and connected with a condenser of known capacity, that previously had been grounded. The drop in the potential caused thereby is observed on the electrometer. From the initial potential and from the potential remaining after closing the condenser, the capacity of the electrometer system may be calculated. The following simple equation will be observed:

$$C_2 : C_1 = (V_1 - V_2) : V_2$$

$C_2$ expresses the capacity of the electrometer system charged to the potential $V_1$, $C_1$ the capacity of the measuring condenser, and $V_2$ the potential of the electrometer after throwing in the condenser.

The condenser for measuring the capacity was a Curie's plate condenser and was constructed in the following manner:

Two glass plates of 50 cm. diameter and 12 mm. thickness, one side of which was chemically silver-plated, served as condenser plates. Both these plates were placed parallel and coaxial to each other with a small distance between. To maintain the distance small pieces of plate glass of exactly the same thickness were placed at the edges of the glass plates at points marked by the ends of an equilateral triangle.

In order to avoid the error that might have arisen by an accidental bending of the glass plates, the lower condenser plate was placed on three supports of hard rubber, each of the same size and at places corresponding to those for the glass-supports. Therefore, a bending of the glass plate would occur in both plates simultaneously, and the distance between them not be changed. A circular layer, 1.5 mm. wide was removed from the silver layer of the upper plate by a compass-like arrangement by means of a copper chisel, thus to construct the protecting ring necessary for the exact calculation of the capacity. The diameter of the inner circular silver layer was 405.7 mm.; the diameter of the outer protection ring was about 5 cm. The upper condenser plate had a hole in the center to render possible a connection to the silver-plating. In the hole, which was also plated with silver, a brass stopper lined with staniol was inserted, to which the connecting

wire was soldered. Care was taken that not a particle of this wire extended over the edge of the silver layer. The entire condenser was placed on a large wooden board and covered with a bell glass through which the necessary conducting wires, well insulated, were inserted. Two bowls filled with calcium chloride, to keep the air dry, were placed so that they could not influence the capacity of the condenser. The insulation of the condenser after repeated moistening with distilled water and careful drying of the condenser plates, proved to be entirely adequate.

For the computation of the capacity we employed the formula of Kohlrausch:

$$C = \frac{(r + r_1)\ 2}{16d}$$

in which r signifies the radius of the collecting plate, $r_1$ the inner radius of the protecting ring, and d the distance of the plate. Inserting the values for our condenser, r = 202.9 mm., $r_1$ = 203.7 mm., and d = 5.38 mm., the capacity is computed to be 1921 cm. The capacity of the wire conductor of the condenser, and the switches, later to be described (see $Z_1$ and $S_1$ in Fig 26), were determined according to the method of Harms and gave 9.9 cm. Thus we obtain for the capacity of the measuring condenser with connecting wiring the value of 1930 cm.

Figure 26 shows the schematic arrangement of the experiment with the sketch of the connections belonging to it. Fig. 27 is a photographic reproduction of the apparatus.

The measuring condenser under the glass bell G was placed on one side of a large table T. The air measuring chamber J with its support H consisting of a three-legged small table, was placed above the condenser. The support H was fastened with screws to the surface of the table in a vertical position by a properly constructed wooden frame $H_1$.

The wiring to the air chamber protruding from the under side of support H was connected on one side with a wire to the connecting post Z of the electrometer, for which purpose we used the rubber cable provided with an electrostatic protection. It was carried from below through the plate of the table and kept in place and position by a proper support of wood. The wiring also was connected with the switch S, which permitted throwing for a short time the measuring condenser by the wire L into the electrometer system. The switch was arranged so that the collector plate of the condenser was grounded before throwing in the electrometer system. Air chamber, wiring and switch were placed in the lead cases $B_1$ and $B_2$, to protect them from the X-rays. The brass tube carrying the leaden diaphragms was the only part of the apparatus that projected out of the lead case. The connecting wiring to the electrometer and the measuring condenser were carried through the lead

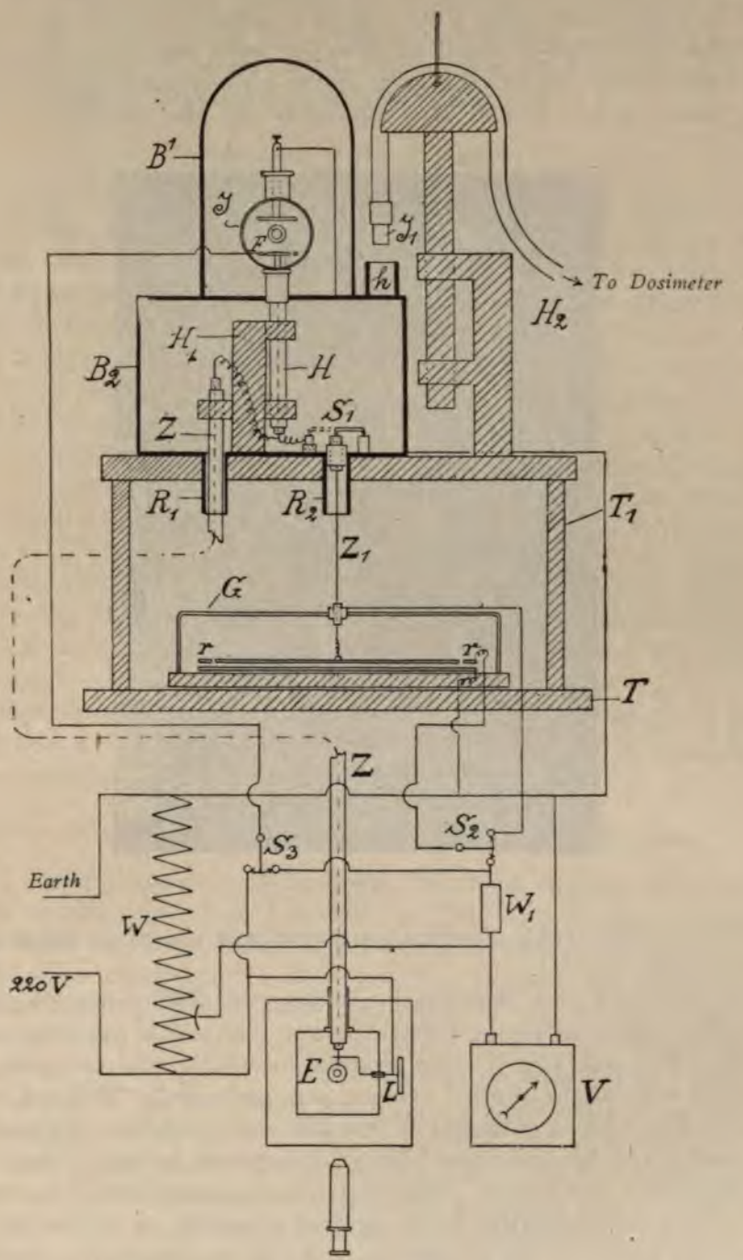
B'
J
J1
h
To Dosimeter
H2
H1
H
B2
S1
Z
R1
R2
T1
Z1
G
r
r1
T
Z
S2
S3
Earth
W
W1
220 V
E
L
V

Fig. 26.

pipes $R_1$ and $R_2$ each 15 cm. long to avoid the entrance of X-rays into the switch chamber. To avoid secondary rays which might arise from X-rays entering the air chamber in the walls of the lead box and thus eventually give rise to sources of error, the X-rays left the lead cases through an attached lead pipe without striking the walls of it. It may be seen in the photographic reproduction. The electrometer E and the apparatus for the activation of the

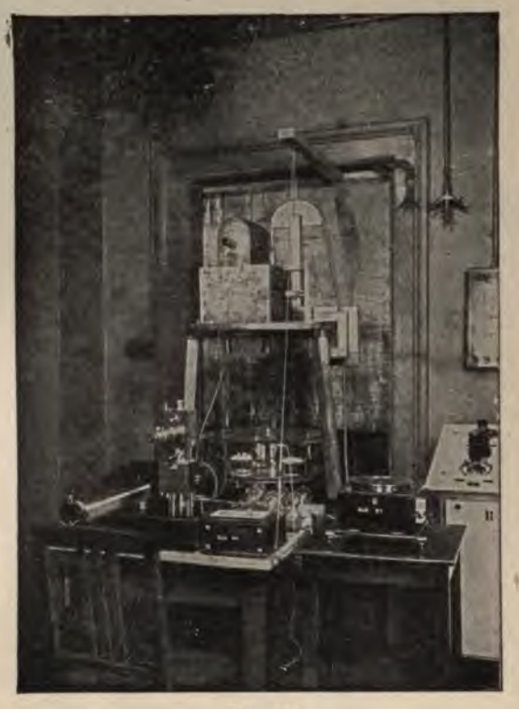

FIG. 27.

necessary measurable electrical potential was placed on the anterior part of the table.

It consisted of a Ruhstraat resistance of 5000 ohms which was directly connected to the electric power plant of a potential of 200 volts. The one side of the system to which was connected the ground wire of the central system, was grounded. Through a controller any desired potential of 0 to 200 volts could be obtained. Its amount could be determined by an interposed normal voltmeter V of Hartmann and Braun. The electrometer system could be charged with the potential switch to the desired potential, or by the two pole changers $S_2$ and $S_3$ the protecting ring r of the measuring condenser could be grounded or changed to the desired potential, or the accessary field F in the air chamber could always be changed to the desired potential. All the protecting covers of the apparatus were grounded by wires soldered to them.

The ionization chamber of the instrument to be standardized was

placed on a wooden frame at the same height with the air chamber and at the same distance from the X-ray tube. As it was necessary during the course of the gauging to exclude the X-rays from this chamber during the time of the recharge of the electrometer system, the chamber could be lowered by means of its support into a leaded bowl h in which it could not be struck by the X-rays.

*Production of the X-Rays*

We used a large inductor with gas interrupter for the production of the X-rays, as X-ray tube a Coolidge tube, the hot cathode of which was heated by a storage battery. Besides a hot cathode ventilation tube an accessary spark gap of 5 cm. was placed in series with the Coolidge tube. The voltage in the tube differed with the different filters. It was the same as previously determined as best suitable with these filters. As it was of the utmost importance that the room in which the gauging apparatus was located should be kept as free as possible from X-rays, from which a source of grave error might arise, the inductor and X-ray tube were placed in an adjoining room. The communicating door was covered with heavy lead plates. The Coolidge tube, which was placed in a bowl of leaded glass, was carried in a wooden stand placed close to the leaded door. A narrow beam of X-rays was directed through an opening of 5 mm. located in the leaden door into the measuring room to the air chamber. The distance from focus to the center of the air chamber was 90 cm.

Through another small opening a few centimeters laterally from the first one, a second radiation beam was directed to the chamber of the dosimeter.

*Determination of the Capacity of the Electrometer System.*

After the electrometer system had been kept charged with the charging arrangement (see Fig. 26), to 200 volts during several hours to avoid the error of the dielectric, the electrodes of the accessary field were brought to the same potential through the switch $S_3$. The protecting ring r and the collector plates of the condenser were grounded through switches $S_2$ and $S_1$. The position of the electrometer needle in the scale of the electrometer was noted. Then through switch $S_1$ the measuring condenser of the electrometer system was closed for as short a time as possible and simultaneously through switches $S_2$ and $S_3$ the protecting ring r and the electrodes of the accessary field F were brought to the potential of the electrometer system, which had been previously determined by experimentation after closing the measuring condensers. The position of the needle of the electrometer system was again read and noted.

The results of six such measurements have been entered in the following table. In the first column the position of the electrometer needle has been recorded before closing the measuring condenser, while in the second column the position of the electrometer needle

after closing the measuring condenser is entered. We see from the numbers that a remarkable conformity of the values exists.

| Position of leaf of electrometer before closure of measuring condensator | Position of leaf of electrometer after closure of measuring condensator |
|---|---|
| — 35.0 | + 1.5 |
| — 35.0 | + 1.5 |
| — 35.0 | + 1.5 |
| — 35.0 | + 1.6 |
| — 35.0 | + 1.5 |
| — 35.0 | + 1.4 |

We could determine through the precision voltmeter V to what potential, expressed in volts, the position of the electrometer needle corresponded. A potential of 217.5 volts was determined before closing the measuring condenser and a mean potential of 115.6 volts after closing the measuring condenser for six readings of the electrometer needle. From these values the capacity of the electrometer system $C_2$ is calculated as

$$C_2 : 1930 = (217.5 - 115.6) : 115.6$$

therefore $C_2$ equals 1700 cm.

A capacity of 1715 cm. respectively 1683 cm. was obtained from two other measurements. Therefore we may take a mean capacity of 1700 cm. for our further experiments.

*Insertion of the Ionization Chamber.*

The insertion of the air chamber and the iontoquantimeter chamber to be standardized with the same into the radiation beam was performed by means of the X-rays. For this purpose the rear cover of graphite paper was replaced with a cover of the same size, the opening however was closed with a barium platinum cyanide screen which was provided with a hole in the center, the size of 1 mm.

The focus of the X-ray tube, the opening in the lead wall as well as both diaphragms of the air chamber were placed in one line by aiming through the small opening in the lead diaphragm. The X-ray tube was then activated. The opening in the anterior lead cover of the air chamber may then be observed as a luminous circle upon the fluorescent screen. By moving the tube in its holder it was possible to bring the small opening, seen as a non-luminous spot in the center of the luminous circle, in an exact alignment with the center of the luminous field. When this was attained then the point source of X-rays on the anticathode was exactly placed in the center of the air chamber. The exact alignment was finally tested by a photographic control.

The alignment of the ionization chamber of the instrument to be standardized was also performed with a luminous screen. The wooden stand which carried the connections as well as this chamber, was moved about until the chamber was located entirely within the

radiation beam passing through the small opening in the lead wall. Care was naturally taken that the distance of the chamber, to be standardized, from the anticathode remained the same as the distance of the middle of the air chamber to the source of radiation.

*The Sources of Errors.*

The sources of errors in the gauging process were identically the same as those previously mentioned in the measurements of the intensity of X-rays and in the description of the iontoquantimeter. Electrostatic disturbances never appear to be disturbing due to the enclosure of the entire electrometer system in grounded metal covers. The leaves or hands of the electrometer of the iontoquantimeter remained completely at rest even if an inductor was operated with a long parallel spark gap without insertion of the X-ray tube. The error, caused by a defective insulation of the electrometer system and the creeping in and leaking out of the charge of the electrometer system in the dielectric of the cable, was determined in the gauging system as well as in the iontoquantimeter to be standardized before and after each test. The disturbances which might have been caused by an undesirable radiation within the measuring room and might have produced an unintentional discharge of the electrometer, were prevented by placing the source of radiation of the X-ray tube in a neighboring room. If the diaphragm of the air chamber was closed by a lead-sheet, or if the ionization chamber of the instrument to be gauged was lowered into the lead bowl, the electrometers were practically at rest during the time duration of a test. Finally we may mention a source of error which could arise from the possibility that the two X-ray beams leading to the ionization chambers would not be of the same intensity, and that with equal distance of both ionization chambers from the source of radiation the intensity of the X-rays striking one of the chambers would be less on account of passing through a thickened portion of the glass wall of the X-ray tube than the X-rays striking the other chamber. This was avoided by placing the tube vertically. The glass wall of an X-ray tube, has an irregular thickness in a plane passing through the electrode, while it is usually of even thickness in a plane vertical to the other. A microscopic measurement of the thickness of the glass walls of the X-ray tube in these two planes as a control confirmed this supposition. The two areas of the glass bulb of the X-ray tube in alignment with the ionization chambers had an even thickness of $\frac{1}{100}$ mm.

Finally we were careful that the X-rays, if filtered, always passed vertically through the filter which was placed close to the roentgen tube.

*Process of the Gauging.*

In order to demonstrate the process of gauging the scale of the iontoquantimeter with the air chamber in electrostatic units we give

in the following a description of and a gauging test from the observation journal:

After all controls for the correct alignment of the X-ray tube and ionization chambers had been made with the fluorescent screen, as described above, the two electrometer systems were charged for several hours to saturate the dielectric. The iontoquantimeter to be gauged was then discharged to the middle of the 15 division scale in as short a time as possible to test the insulation and dielectric error. The behavior of the needle of the electrometer was observed during one and a half hours. This time was required for gauging, as earlier tests have shown. The position of the electrometer needle was observed for every five minutes and finally for longer time intervals. The results and the readings are compiled in the following table and Fig. 28.

| Time | 0′ | 5′ | 10′ | 15′ | 20′ | 25′ | 30′ | 46′ | 60′ | 92′ |
|---|---|---|---|---|---|---|---|---|---|---|
| Position of needle of electrometer ..... | 7.3 | 7.0 | 6.8 | 6.4 | 6.2 | 6.15 | 6.05 | 5.8 | 5.75 | 5.8 |

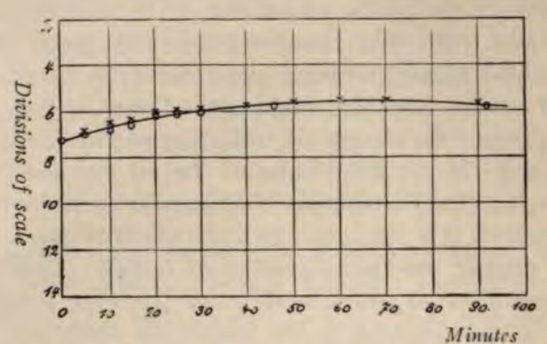


FIG. 28.—Insulation-resp. dielectric error of the iontoquantimeter to be regulated.

The values of the table have been plotted in Fig. 28. They are designated with 0. We see quite a similar course as in Fig. 20 which represents the compilation of the errors of insulation and the dielectric of the iontoquantimeter.

Next the determination of the error of the insulation and the dielectric of the electrometer system of the testing apparatus was made.

During this test the movement of the electrometer leaf to 5 divisions of the scale was observed. Therefore the error was determined in the manner that after a saturation of the dielectric the electrometer system was rapidly discharged by 2.5 divisions of the scale and the position of the electrometer leaf was observed during the duration of 10 minutes. Previous tests had shown that the time in which the gauging system was discharged for 5 divisions of the scale was always attained within 10 minutes. The execution of the measurement revealed that the error of insulation and dielectric amounted to 0.7 division of the scale within 10 minutes.

After the determination of the error the standard instrument and the iontoquantimeter to be gauged were again kept in a charged state for some time. Then the X-ray tube was placed in operation and set at the desired hardness corresponding to a parallel spark gap of 30 cm.—we are describing a gauging with X-rays filtered with 3 mm. aluminum—by regulating the hot cathode current and the primary current. The operation was continued for some time until control tests showed that the tube had become constant.

The air chamber and the chamber of the iontoquantimeter were exposed at the same time to the action of the X-rays. The electrometer of the standard apparatus was observed until the electrometer leaf had passed through five divisions of the scale. The moment this occurred, the ionization chamber of the iontoquantimeter was lowered into the protecting bowl h, Fig. 26. The time used for this was noted. The position of the needle on the iontoquantimeter was observed on the scale and also recorded. After this the electrometer system of the standard apparatus was again charged, mostly one division beyond the five divisions serving for the measuring. As soon as the leaf of the electrometer touched 0 of the scale the ionization chamber of the iontoquantimeter was again placed in the raybeam and thereby exposed to the action of the X-ray until five divisions of the scale were again discharged. The entire scale of the iontoquantimeter was gauged in this manner. The same potential had been applied to the accessary field of the air chamber at the beginning of the measuring series as the electrometer system held at the beginning of the measuring. As the potential of the electrometer system decreases during the measuring, the potential of the accessary field was gradually adjusted corresponding to the potential of the electrometer system to avoid errors by regulating the resistance in the potential diviser.

The values of each measurement of the gauging are recorded in the following table. In the first column are the values of the discharge of the gauging system for each five divisions of the scale, in the second column the time values consumed, and in the third column the position of the needle of the electrometer of the iontoquantimeter in values of its scale.

| Number of discharge of the adjusting instrument | Time duration of discharge | Position of hand of electrometer to the hand of iontoquantimeter |
|---|---|---|
| 1 | 6′30″ | 0.5 |
| 2 | 6′11″ | 1.1 |
| 3 | 5′56″ | 2.4 |
| 4 | 5′54″ | 3.8 |
| 5 | 6′37″ | 5.8 |
| 6 | 6′09″ | 8.2 |
| 7 | 6′35″ | 10.1 |
| 8 | 7′02″ | 12.0 |
| 9 | 6′41″ | 13.4 |
| 10 | 6′20″ | 14.9 |
| 11 | 6′22″ | 15.0 |

We see from this table that the single divisions of the scales of the iontoquantimeters obtained in the trade are not equivalent. The incorrectness is especially marked in the first part of the scale.

Following this measuring series both electrometer systems were again charged to the zero value of the scales. The insulation and dielectric errors were again determined in an analogous manner as described in the preceding paragraphs. The following values were obtained for the iontoquantimeter:

| Time in minutes | 0′ | 5′ | 10′ | 15′ | 20′ | 25′ | 30′ | 40′ | 50′ | 73′ | 90′ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Position of hand of electrometer ..... | 7.3 | 6.85 | 6.5 | 6.3 | 6.0 | 5.95 | 5.9 | 5.75 | 5.6 | 5.5 | 5.6 |

The values are designated with + in Fig. 28, and conform quite well to the first values.

A value of 0.9 for one division of the scale was found this time for the insulation and dielectric error of the gauging apparatus.

We can calculate the amount of electricity in the ionization chamber in electrostatic units, as we know the capacity of the electrometer system. The potential of the gauging system expressed in volts is 220 with the zero position of the scale, 206.4 with the position of the needle at the scale division at 5. We therefore obtain for the discharge in electrostatic units.

$$\frac{C\ (V-V_1)}{300} = 1700\ .\ \frac{(220-206.4)}{300} = 7.72\ e$$

The mean duration of discharge for five divisions of the scale of the gauging system amounted to 6.24″. The error of insulation and dielectric for this discharge time represents a value of 0.5 division of the scale.

Applying the correction the 7.72 e value is changed to 6.94 e.

The volume of the measuring chamber is 4.38 ccm. Therefore the quantity of electricity per ccm. air of the ionization chamber with the discharge of five divisions of the scale is 6.94 : 4.38 = 1.58 e. Ten discharges of the five scale divisions and one discharge of 0.7 scale division were required within a time of 70 minutes for the entire 15 divisions of the scale of the iontoquantimeter.

The entire 15 divisions of the scale of the iontoquantimeter therefore correspond to a dose of 15.86 e. The error of insulation and dielectric of the iontoquantimeter during this time was 1.5 divisions of the scale. The error was of such a magnitude that the electrometer system required an additional quantity of electricity corresponding to 1.5 divisions of the scale caused by the leaking out of the charge through the dielectric after a discharge of one-half of the scale. The error influences the result in the sense that the quantity of electricity determined by the gauging apparatus during the discharge of the iontoquantimeter appears to be 10 per cent too high. The final result therefore is 14.2 and not 15.86 e.

Two additional measurements with the same quality of rays resulted in a final value of 15.2 e, respectively 14.2 e for the entire scale

of the dosimeter. The values therefore are sufficiently equivalent for our purposes.

We also performed a gauging of the iontoquantimeter with harder and softer rays, that is, with X-rays filtered with 1 mm. copper and unfiltered X-rays. The results of these measurements gave values for the dose of the entire scale of the iontoquantimeter of 14.6 and 15.3 which again were closely equivalent to the values obtained from X-rays filtered with 3 mm. aluminum. The uniformity of the results of measurements from different qualities of rays may be regarded as a further proof that the graphite chamber of the iontoquantimeter enables one to obtain a comparative dosation for biologic purposes free from any objections.

By means of the recorded readings of the single discharges of the gauging apparatus on the scale of the iontoquantimeter it becomes an easy matter to transcribe the scale in electrostatic units per ccm. of air.

The dependence of the dosimeter has been tested by determining from time to time with our source of constant gamma radiation the time duration of a discharge of the electrometer system. It is self-evident that we observed during each measurement that the ionization chamber was always placed in the same position to the source of radiation. A stand specially constructed for the purpose facilitated this with minutest exactness.

In the following table the results of these tests have been entered. In the first column are the dates of the days of the test within one year, while in the second and third columns are entered the times observed for two of our dosimeters. We conclude from the results that the times of discharges do not appreciably vary in spite of the relatively long time interval between the various measurements.

| Day of testing | Iontoquantimeter 1 | Iontoquantimeter 2 |
|---|---|---|
| 12. March | 38′ | 46′ |
| 28. March | 36′ | 48′ |
| 24. April | 38′ | 45′ |
| 30. June | 36′ | 46′ |

The sensitiveness of the instrument also has been tested with the result that it is quite sufficient for biologic purposes for the sensitiveness of the biologic object to the action of gamma-rays is rather slight, as will be seen from the investigations recorded in the second part of the book. Most of the biologic objects react with a visible difference to the intensity of the biologic action only after a difference of about 20 per cent in the dosages has been attained.

### *Investigations Concerning the Sensitiveness and Dependence of the Kienböck Strips.*

The sensitiveness and dependability of our modified iontoquantimeter had been tested by using radium and mesothorium as a constant source of radiation. We saw that the instrument answers to

all demands that we might require from a dosimeter in a far-reaching manner. We, therefore, used the iontoquantimeter to compare other dosimeters with it and to test their sensitiveness and dependence. As the Kienböck strips and the Sabouraud-Noiré tablets show readable reactions only after a very long exposure to gamma-rays of even large intensities, we made use of the X-rays of various hardnesses to test these two dosimeters.

We performed the comparison of dosimeters so that we exposed the ionization chamber, the Kienböck strips and the Sabouraud-Noiré tablets to the X-rays at the same distance from the source of radiation and during the same time.*

We used the same hardnesses of rays as in the experiments made previously. We chose as the dose 5 e in one series, and 30 e in a second one for the Kienböck strips. To attain a satisfactory discoloration of the Sabouraud-Noiré pastilles we chose a dose of 75 e for the various qualities of rays.

We took special care in the development of the Kienböck strips to employ the most careful chemical treatment. The strips were fastened to a glass plate by rubber bands. By means of a plate-holder they were all immersed at the same time in the developer of the prescribed temperature and finally fixed within the same time. All sources of errors which might arise from the chemical treatment were avoided.

The Sabouraud-Noiré pastilles were estimated with a Holzknecht dosimeter with an ordinary electric carbon globe as well as with a special lamp.

The data for the Sabouraud-Noiré tablets are entered in the following table, while those for the Kienböck strips may be seen in Plate I, Fig. 1, at the end of the book.

TABLE

| Quality of rays | Dose | Value in H determined by Holzknecht-Dosimeter |
|---|---|---|
| Unfiltered X-rays | 75 e | 1.5—1.75 |
| X-rays filtered with 3 mm. aluminum | 75 e | 1.5—1.75 |
| X-rays filtered with 10 mm. aluminum | 75 e | 1.5—1.75 |
| X-rays filtered with 1 mm. cu | 75 e | 1.5—1.75 |
| Gamma-rays | 75 e | Discoloration not of sufficient intensity for determination |

As may be seen from the tables, the investigations show that the blackening of the Kienböck strips and the change in color of the Sabouraud-Noiré tablets do not evince any differences within these considerable variations of hardness. The gamma-rays make an exception, as the strips are very little blackened with their use. A dose measured with the iontoquantimeter tallied with a definite reaction

* According to the directions accompanying the Holzknecht dosimeter, the Sabouraud-Noiré tablets should have been placed at the half focal distance from the source of radiation. We deemed it better for the purpose of comparison to place the three dosimeters at the same distance, thus to guard against sources of errors from secondary rays of the tube-holder, filters, and so forth.

of the Kienböck strip and change of color of the Sabouraud-Noiré tablets, it did not matter whether we used soft or hard rays.

One might draw the conclusion that the doubts which we already expressed about the reagents used in the Kienböck strips and the Sabouraud-Noiré tablets would become obsolete, but we shall see immediately that this uniformity of reaction is only an apparent one, due to the marked insensibility of the two dosimeters. To test the sensitiveness of the dosimeters we exposed a number of Kienböck strips and Sabouraud-Noiré tablets to X-rays of a known hardness and applied differently strong doses measured with the iontoquantimeter in differences of about 50 per cent. The results of these tests are entered in the following table for the Sabouraud-Noiré tablets and in Fig. 2, Plate I. for the Kienböck strips.

| Dose | 75 e | 115 e | 150 e |
|---|---|---|---|
| Value in H Holzknecht-Dosimeter ..... | 1.5—1.75 | 1.5—1.8 | 2.0—2.5 |

We see from the table and Fig. 2, Plate I, that the sensitiveness of both dosimeters is indeed a very slight one. With a difference of 50 per cent in the dose we may determine a difference in the blackening of the Kienböck strips and with about the same difference in the Sabouraud-Noiré tablets. Frequently repeated measurements gave the same results.

The reliability of these dosimeters is not pronounced. The sensibility of one photographic sheet shows differences at various regions of more than 50 per cent. We also have frequently observed that a given number of Kienböck strips, which had received the same dose and had been developed alike and carefully, showed marked differences of blackening which according to the sensibility determination would amount to more than 50 per cent of the dose.

### *Investigations of the Sensitiveness and Dependence of the Fürstenau Intensimeter.*

The change of resistance of the selenium cell of the Fürstenau intensimeter by the action of roentgen-rays, and the degree of the change of resistance serve as measure of the intensity.

We defined intensity as the radiation energy striking 1 sq. cm. of surface within a second. As the degree of the change of resistance of selenium is evidently dependent on the amount of the absorbed radiation energy one does not measure the intensity by the change of resistance of selenium but the intensity divided by the half absorption value layer. The use of the Fürstenau intensimeter with the same kind of radiation is not objectionable when measuring the relative intensity. However, in practical use a disturbing factor may be observed, namely, the selenium cell tires during frequent or long exposures.

The selenium cell after a certain time recuperates to its original sensitiveness. So if the selenium cell has recuperated from the previous radiation the instrument again gives correct values of short-

time measurements. For short measurements, for instance in diagnosis, the intensimeter is very useful.

This tendency to tire is fraught with difficulties if we use the intensimeter as dosimeter. If we intend to use the intensimeter as dosimeter then we proceed according to the definition of dose in such a manner that one determines the deflection of the instrument within definite time intervals. From these values the time is calculated that is necessary to obtain a definite dose. The factor of exhaustion must be especially disturbing in these calculations as the time intervals are not to be too great on account of the inconstancy of the tube. All in all the error of measuring may be slight when a Coolidge or Lilienfeld tube is used. They are characterized by a relatively high constancy. Therefore the measurements may be taken within sufficiently large time intervals. Employing one and the same quality of rays and one and the same filter, the instrument is usable with such radiations. However, as soon as we intend to compare doses of varying qualities of rays with each other, the instrument must disappoint on account of the inconstancy of the absorption in selenium in comparison to that in the biologic body. To prove this also mathematically we undertook comparative tests with the intensimeter and the iontoquantimeter by exposing both, the ionization chamber and the selenium cell, to the rays at the same distance from the point source of radiation. Using the gamma-rays we arranged by a marked sliding device that the selenium cell of the intensimeter always came to lie in the same place as the ionization chamber of the iontoquantimeter. The results have been compiled in the following table.

| Hardness of rays | 5 units of scale of electrometer in seconds | Deflection of intensimeter in F | Ratio of intensities |
|---|---|---|---|
| Unfiltered X-rays | 9.0″ | 7.8 | 1.21 |
| X-rays filtered with 3 mm. aluminum | 9.0″ | 10.5 | 0.94 |
| X-rays filtered with 10 mm. aluminum | 8.6″ | 11.3 | 0.91 |
| X-rays filtered with 1 mm. cu. | 10.8″ | 8.15 | 1 |
| Gamma-rays | 102 | 0.25 | 0.18 |

The table shows, as was to be expected from the comparative measurements of selenium and water, that without any further consideration the intensimeters of Fürstenau, cannot be used as a dosimeter if a comparative dosation of various hard rays is intended.

We do miss the systematic dependability of the measured values from the hardness as they were obtained from the measurements of absorption in selenium. We cannot at present decide to what this may be traced as we were not familiar with the interior construction of the chamber in the construction of which also other metals besides selenium might have been used.

The sensibility of the intensimeter for measuring radiations is amply sufficient for biologic purposes for which the instrument is intended. It is by all means considerably larger than that of the Kienböck strips or the Sabouraud-Noiré tablets.

The dependability of the instrument has been tested in quite a similar manner as for the iontoquantimeter by means of our constant gamma radiation source, and it was found that the values compared quite well with each other. The measurements were performed within time intervals of several months. The differences in the measured values do not surpass 5 per cent of the mean average.

## The Importance of the Secondary Radiation for the Dose

The dosimeter described by us makes it possible, on account of the construction of the ionization chamber, to determine the dose not only on the surface of the body but also in the depth, that is, in the interior of body cavities, if they possess a sufficiently large communication with the outer world. We will observe in the biologic

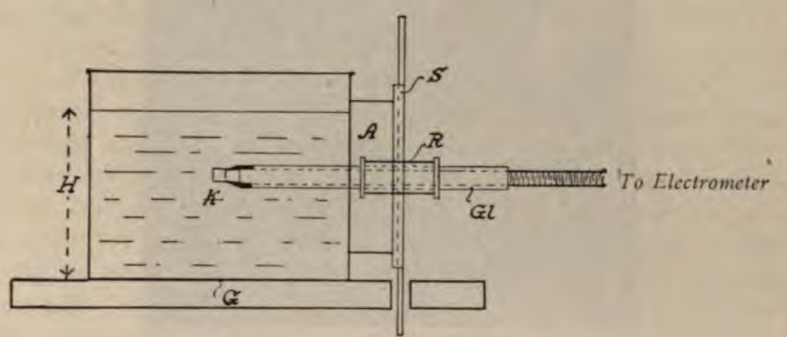


Fig. 29

part of this book the great advantages these measurements possess when taken at the regions of the body where we intend to apply a definite dose. In many instances it is unfortunately impossible to insert the dosimeter chamber at the place in the interior of the body where the dose must be determined.

In order to obtain an idea of the value of the actual dose applied in the depth, it has been attempted to determine the depth dose by calculations from the surface dose, the half absorption value layer and the law of squares. The dose on the surface of the body was measured with any one of the customary dosimeters. The half absorption value layer of the radiation was determined with Christen's half absorption value layer measure. The decrease of the intensity of the radiation with distance was calculated according to the law of squares.

In certain instances by the use of our dosimeter and ionization chamber we were in a position to compare the depth dose determined by calculations with those obtained from direct measurements. We found that quite marked differences existed between the calculated and the measured dose. Naturally the question arose how this difference between calculated and measured dose could be explained. We had observed the great importance of secondary radiations in

time measurements. For short measurements, for instance in diagnosis, the intensimeter is very useful.

This tendency to tire is fraught with difficulties if we use the intensimeter as dosimeter. If we intend to use the intensimeter as dosimeter then we proceed according to the definition of dose in such a manner that one determines the deflection of the instrument within definite time intervals. From these values the time is calculated that is necessary to obtain a definite dose. The factor of exhaustion must be especially disturbing in these calculations as the time intervals are not to be too great on account of the inconstancy of the tube. All in all the error of measuring may be slight when a Coolidge or Lilienfeld tube is used. They are characterized by a relatively high constancy. Therefore the measurements may be taken within sufficiently large time intervals. Employing one and the same quality of rays and one and the same filter, the instrument is usable with such radiations. However, as soon as we intend to compare doses of varying qualities of rays with each other, the instrument must disappoint on account of the inconstancy of the absorption in selenium in comparison to that in the biologic body. To prove this also mathematically we undertook comparative tests with the intensimeter and the iontoquantimeter by exposing both, the ionization chamber and the selenium cell, to the rays at the same distance from the point source of radiation. Using the gamma-rays we arranged by a marked sliding device that the selenium cell of the intensimeter always came to lie in the same place as the ionization chamber of the iontoquantimeter. The results have been compiled in the following table.

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| Gamma-rays | 102 | 0.25 | 0.18 |

The table shows, as was to be expected from the comparative measurements of selenium and water, that without any further consideration the intensimeters of Fürstenau, cannot be used as a dosimeter if a comparative dosation of various hard rays is intended.

We do miss the systematic dependability of the measured values from the hardness as they were obtained from the measurements of absorption in selenium. We cannot at present decide to what this may be traced as we were not familiar with the interior construction of the chamber in the construction of which also other metals besides selenium might have been used.

The sensibility of the intensimeter for measuring radiations is amply sufficient for biologic purposes for which the instrument is intended. It is by all means considerably larger than that of the Kienböck strips or the Sabouraud-Noiré tablets.

The dependability of the instrument has been tested in quite a similar manner as for the iontoquantimeter by means of our constant gamma radiation source, and it was found that the values compared quite well with each other. The measurements were performed within time intervals of several months. The differences in the measured values do not surpass 5 per cent of the mean average.

## The Importance of the Secondary Radiation for the Dose

The dosimeter described by us makes it possible, on account of the construction of the ionization chamber, to determine the dose not only on the surface of the body but also in the depth, that is, in the interior of body cavities, if they possess a sufficiently large communication with the outer world. We will observe in the biologic

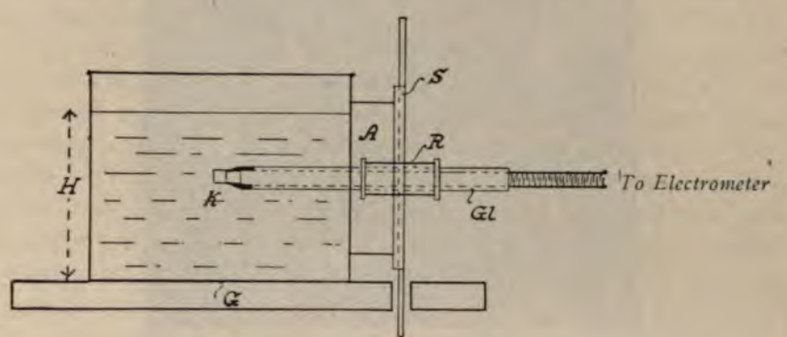


Fig. 29

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In order to obtain an idea of the value of the actual dose applied in the depth, it has been attempted to determine the depth dose by calculations from the surface dose, the half absorption value layer and the law of squares. The dose on the surface of the body was measured with any one of the customary dosimeters. The half absorption value layer of the radiation was determined with Christen's half absorption value layer measure. The decrease of the intensity of the radiation with distance was calculated according to the law of squares.

In certain instances by the use of our dosimeter and ionization chamber we were in a position to compare the depth dose determined by calculations with those obtained from direct measurements. We found that quite marked differences existed between the calculated and the measured dose. Naturally the question arose how this difference between calculated and measured dose could be explained. We had observed the great importance of secondary radiations in

time measurements. For short measurements, for instance in diagnosis, the intensimeter is very useful.

This tendency to tire is fraught with difficulties if we use the intensimeter as dosimeter. If we intend to use the intensimeter as dosimeter then we proceed according to the definition of dose in such a manner that one determines the deflection of the instrument within definite time intervals. From these values the time is calculated that is necessary to obtain a definite dose. The factor of exhaustion must be especially disturbing in these calculations as the time intervals are not to be too great on account of the inconstancy of the tube. All in all the error of measuring may be slight when a Coolidge or Lilienfeld tube is used. They are characterized by a relatively high constancy. Therefore the measurements may be taken within sufficiently large time intervals. Employing one and the same quality of rays and one and the same filter, the instrument is usable with such radiations. However, as soon as we intend to compare doses of varying qualities of rays with each other, the instrument must disappoint on account of the inconstancy of the absorption in selenium in comparison to that in the biologic body. To prove this also mathematically we undertook comparative tests with the intensimeter and the iontoquantimeter by exposing both, the ionization chamber and the selenium cell, to the rays at the same distance from the point source of radiation. Using the gamma-rays we arranged by a marked sliding device that the selenium cell of the intensimeter always came to lie in the same place as the ionization chamber of the iontoquantimeter. The results have been compiled in the following table.

| Hardness of rays | 5 units of scale of electrometer in seconds | Deflection of intensimeter in F | Ratio of intensities |
|---|---|---|---|
| Unfiltered X-rays | 9.0″ | 7.8 | 1.21 |
| X-rays filtered with 3 mm. aluminum | 9.0″ | 10.5 | 0.94 |
| X-rays filtered with 10 mm. aluminum | 8.6″ | 11.3 | 0.91 |
| X-rays filtered with 1 mm. cu. | 10.8″ | 8.15 | 1 |
| Gamma-rays | 102 | 0.25 | 0.18 |

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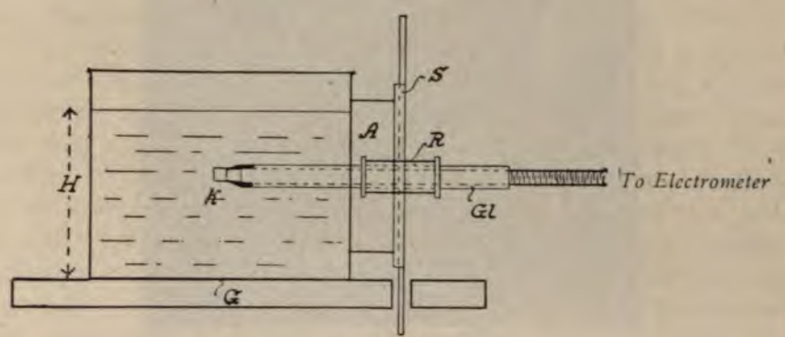


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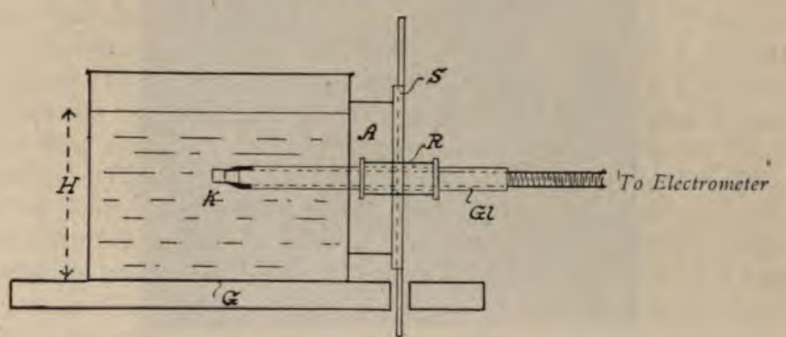


Fig. 29

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the measurements for determining absorbability and it was clear that this difference could only be caused by secondary radiations. We could not make use of the human body to investigate the influence of the secondary radiation on the dose and its proportion in comparison to the primary radiation. We therefore constructed a water phantom for these investigations, as we had proven the equality of absorbability of water with that of human tissue.

The phantom (see Fig. 29) consisted of a cylindrical vessel G made of sheet iron of a diameter of 35 cm. and a height of 25 cm.

Fig. 30

It was usually filled with water to a height (H) of 20 cm. The ionization chamber K was inserted laterally to the middle of the vessel. To be able to place the measuring chamber in the water at various heights or depths, without changing the level of the surface of the water, the following arrangement was made:

A tin piece A was joined to the lateral wall of the vessel, which was closed with metal slides S. To the center of the metal slides a brass pipe R was soldered. A glass pipe Gl was inserted into the brass tube and rendered watertight by rubber rings. The cable leading to the measuring chamber K was inserted through the glass tube. The measuring chamber K protruded beyond the glass tubing into the interior of the vessel. The space between glass tube and chamber was rendered watertight by filling the space with wax. The chamber also was protected with a thin layer of wax against the entrance of water into its interior. The dimensions of the slider permitted to change the position of the chamber from the surface to a depth of 10 cm. The position of the chamber could be read from a scale attached to the slider. A catch-spring adjustment also was provided on the slider for rapid adjustment of the position of the chamber which caught from centimeter to centimeter. Fig. 30 shows the phantom in a photographic reproduction.

*Comparison between the Depth Dose calculated from the Surface Dose and the Depth Dose measured in the Water Phantom.*

We performed the comparison with X-rays filtered with 1 mm. copper and selected a port of entry of 15 sq. cm. The anticathode of the roentgen tube, which was placed in a bowl lined with leaded rubber was placed 50 cm. above the surface of the water. The desired size of the field was attained by an adjustable diaphragm at the base of the tube holder. The copper filter was placed close beneath the bowl. Two methods of measuring may be considered: The one consists in measuring a known dose on the surface and then determine the dose which is obtained in the depth within the same time. The method presupposes that the electrometer possesses a proportionality determinable from the scale. The other method is to take the time in which a known dose is attained at the surface and then determine the time within which the same dose is obtained in the depth. In the second method it is not necessary to obtain a proportionality of the doses, as at each reading the needle of the electrometer travels over the same space of the scale. In this instance the surface dose and the depth dose are in an inverse ratio to the times of reading. We chose the second method, as the two leaf electrometer of Wulf, used for these experiments, did not possess a proportionality for the deflection of the scale and we would have been compelled to undertake a new gauging of the scale prior to each test if we had used the first method. The measurements were carried out so that we determined alternately at the surface and in the depth several times successively the time within which the leaf of the electrometer connected to the measuring chamber passed through five divisions of the scale. We previously determined through a few readings that the roentgen tube was constant. We give the following values as an example of such a measurement.

| Method of measuring | 5 units of scale of electrometer in seconds |
|---|---|
| Surface | 54.2 |
| 10 cm. depth | 122.0 |
| Surface | 52.8 |
| 10 cm. depth | 124.0 |
| Surface | 52.4 |
| 10 cm. depth | 125.0 |

We obtain in per cent of the surface dose a depth dose of 43 per cent.

The half absorption value layer of X-rays filtered with 1 mm. copper was 3.7 cm. determined with exact physical methods. The distance of the focus to the surface was 50 cm., to depth 60 cm. If we calculate the depth dose from the half absorption value layer and the law of dispersion, then we obtain a value of only 10 per cent of the dose measured on the surface.

This example demonstrates the marked difference of the measured dose and the influence of secondary rays on the dose.

All tables and graphs for the calculation of the dose from the half absorption value layer and from the distance of the object from the source of radiation, recorded in text books on deep roentgen therapy require correction, as in them the great influence of the secondary radiation on the dose has not been taken into account.

To obtain an idea of the size of this error, which is inherent in such a calculated table or graph, we have determined the decrease of the dose in the depth from centimeter to centimeter with the same size of field as in the previous tests and compared the values found with the values obtained by calculation.

The course of the experiment conformed closely to the preceding one. The distance of the focus of the Coolidge tube from the surface was 50 cm., the filters used were 10 mm. aluminum and 1 mm. copper. The measurement was carried out so that the measuring chamber of the dosimeter was lowered in the water phantom 1 cm. each time. A surface measurement was always taken between each depth measurement as a control. The results recorded in the following table have been gained from X-rays filtered with 10 mm. aluminum. In column one the methods of measurement are stated, in column two the time durations in seconds of the discharge of 5 units of the scale of the electrometer, in the third the measured values of the depth dose in per cent of the surface dose, while in the last column the values calculated from the half absorption value layer and the law of dispersion in per cent of the surface dose have been entered.

X-RAYS FILTERED WITH 10 MM. ALUMINUM

| Method of measuring | 5 units of scale of electrometer in seconds | Measured values of depth dose | Values of depth dose in % of surface dose calculated from half value absorption layer and dispersion |
|---|---|---|---|
| 0 cm. depth..... | 23.8 | 100% | 100% |
| 1 " " ..... | 24.4 | 89% | 81% |
| 0 " " ..... | 23.8 | | |
| 2 " " ..... | 27.4 | 87% | 63% |
| 0 " " ..... | 23.8 | | |
| 3 " " ..... | 31.2 | 77% | |
| 0 " " ..... | 24.2 | | |
| 4 " " ..... | 35.4 | 69% | 37% |
| 0 " " ..... | 24.4 | | |
| 5 " " ..... | 39.4 | 60% | |
| 0 " " ..... | 23.0 | | |
| 6 " " ..... | 46.2 | 51% | 22% |
| 0 " " ..... | 23.8 | | |
| 7 " " ..... | 50.0 | 47% | |
| 0 " " ..... | 23.0 | | |
| 8 " " ..... | 56.0 | 42% | 13.8% |
| 0 " " ..... | 23.6 | | |
| 9 " " ..... | 64.4 | 37% | |
| 0 " " ..... | 23.2 | | |
| 10 " " ..... | 76.0 | 31% | 8.4% |
| 0 " " ..... | 23.8 | | |

Fig. 31, represents the mean values of a series of such measurements in a graph.

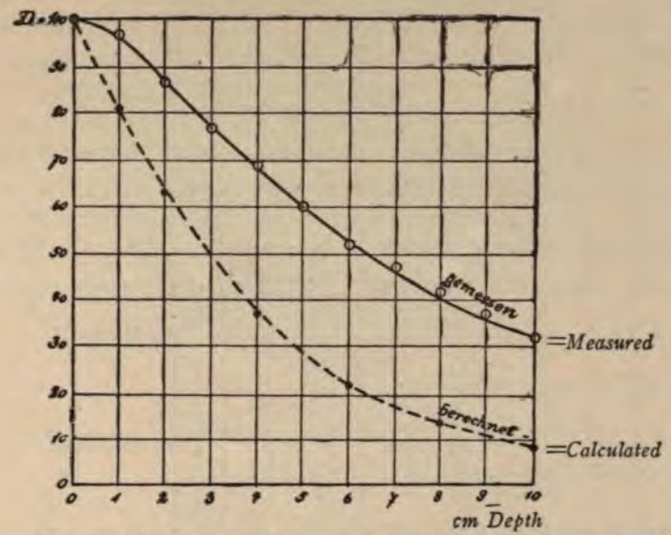



FIG. 31.—Calculated and measured depth dose of X-rays filtered with 10 mm. Aluminum and port of entry of 15 sq. cm.

The following table gives the measurements which were obtained from X-rays filtered with 1 mm. copper.

X-RAYS FILTERED WITH 1 MM. OF COPPER

| Method of measuring | 5 units of scale of electrometer in seconds | Measured values of depth dose | Values of depth dose in % of surface dose calculated from half value absorption layer and dispersion |
|---|---|---|---|
| 0 cm. depth..... | 36.0 | 100% | 100% |
| 2 " " ..... | 39.0 | 96% | 65% |
| 0 " " ..... | 35.4 | | |
| 4 " " ..... | 43.0 | 82% | 40% |
| 0 " " ..... | 35.0 | | |
| 6 " " ..... | 50.5 | 67.5% | 25% |
| 0 " " ..... | 33.0 | | |
| 8 " " ..... | 64.5 | 54% | 17% |
| 0 " " ..... | 37.0 | | |
| 10 " " ..... | 79.5 | 44% | 10% |
| 0 " " ..... | 33.0 | | |

Fig. 32, also illustrates the graph of these values.

These investigations demonstrate the great differences between measured and calculated values.

*A depth dose cannot be calculated from the half absorption value layers and the law of distance. If the dose cannot be directly determined in the depth by inserting the measuring chamber of the iontoquantimeter, then the only practical method for the determination of the dose in the desired depth consists in the use of the water phantom*

*maintaining during the measurements the same conditions as are present in the therapeutic radiation.**

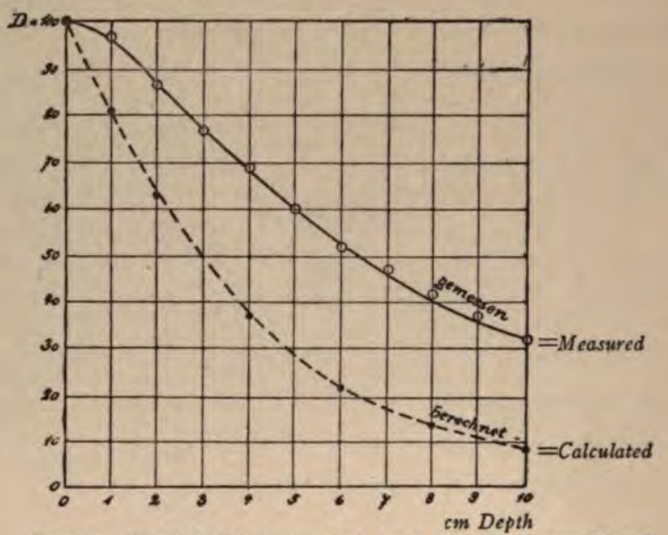



FIG. 32.—Calculated and measured depth dose of X-rays filtered with 1 mm. copper and port of entry 15 sq. cm.

### *Determination of the Absolute Amount of Secondary Radiation with the Water Phantom.*

A dose measured in the water phantom is composed of two factors, namely, the dose obtained from the rays directly emitted from the X-ray tube and the amount of secondary radiations arising from the surrounding regions of the radiated water.

To obtain an idea of the actual size of the proportion of these two factors, of which the dose is composed, we have made the following investigations.

We could not investigate all the many varied possibilities as it is self-evident that the proportional values depend on the choice of the depth, the size of the field, the hardness of rays and other factors. We selected a special instance which conformed to the details maintained in the biologic observations. We chose a port of entry of 15 sq. cm. and a depth of 8 cm.

The anticathode of the roentgen tube, in this instance a Lilienfeld tube, was kept at a distance of 50 cm. from the surface of the water in the phantom. (See Fig. 33.) A radiation beam was obtained by means of an adjustable diaphragm at the bottom of the bowl, which measured 15 sq. cm. on the surface of the water. The filter was placed directly beneath the tube carrier. Aluminum filters of 3 and 10 mm. and a copper filter of 1 mm. were used.

* Note at time of correction of the manuscript: Even in more recent writings as Seuffert: "Radiation Deep Therapy, Experimental and Critical Investigations Concerning their Use in Gynecology," and Küpferle and Lilienfeld: "Principles of the Application of the X-rays," the view is defended that a depth dose may be solely calculated from the half absorption value layer and the dispersion of the rays with distance.

The measuring chamber K of the dosimeter was placed 8 cm. beneath the surface of the water exactly in the center of the field.

The course of the experiment was as follows: The time was ascertained in which the leaf of the electrometer passed five divisions of the scale when the entire radiation beam entered the water phantom through the field of 15 cm. square.

To exclude the secondary rays, which entered the measuring chamber through the radiated water from all sides with this size of field, a heavy lead diaphragm B was placed on the surface of the water which covered the entire field with the exception of the small field 0 in the center of the size of 1 sq. cm. The radiation beam could only strike the measuring chamber. The time was read in

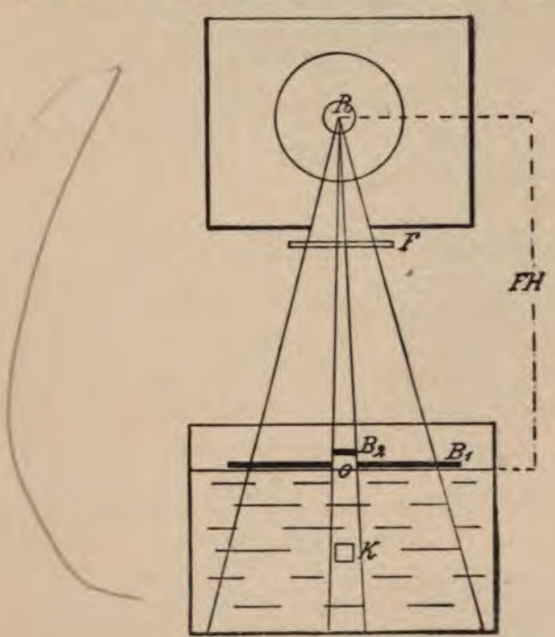



FIG. 33.

which the electrometer leaf passed through five divisions of the scale. The ionization current, now measured, was almost entirely due to the X-rays striking the chamber directly. The secondary rays originating above and beneath the narrow water column and entering the chamber are of such a small intensity in comparison to the secondary rays entering the chamber from all sides with an open field, that they may be neglected.

To exclude the rays which strike the measuring chamber directly and to permit the secondary rays only to enter the ionization chamber a lead diaphragm $B_2$ of the size of 1 sq. cm. was placed so that the small square field 0 in the center was cut out from the total radiation. The time was determined within which the leaf of the electrometer passed through five divisions of the scale.

A series of such measurements have been entered in the following

table. The various measurements have been recorded in their time sequence. As the tube remained constant in all the tests, respectively, the slight deviations in constancy could be taken into account by control measurements, the three values to be measured are inversely proportional to the time values.

X-RAYS FILTERED WITH 3 MM. ALUMINUM

| Method of measuring | 5 units of scale of electrometer in seconds | Primary radiation in % of total radiation | Secondary radiation in % of total radiation |
|---|---|---|---|
| Total radiation ..... | 12.0 | | |
| Primary radiation .... | 43.2 | | |
| Total radiation ..... | 11.8 | | |
| Secondary radiation ... | 16.0 | | |
| Total radiation ..... | 12.0 | | |
| Primary radiation .... | 42.2 | 29.8% | 76.2% |
| Total radiation ..... | 12.2 | with correction for | with correction for |
| Secondary radiation ... | 17.2 | accidental radiation | accidental radiation |
| Total radiation ..... | 12.0 | and so forth | and so forth |
| Primary radiation .... | 42.6 | 25% | 75% |
| Total radiation ..... | 12.0 | | |
| Secondary radiation ... | 16.8 | | |
| Total radiation ..... | 13.4 | | |

X-RAYS FILTERED WITH 10 MM. ALUMINUM

| Method of measuring | 5 units of scale of electrometer in seconds | Primary radiation in % of total radiation | Secondary radiation in % of total radiation |
|---|---|---|---|
| Total radiation ..... | 15.0 | | |
| Primary radiation .... | 42.0 | | |
| Total radiation ..... | 15.0 | | |
| Secondary radiation .. | 18.0 | | |
| Total radiation ..... | 15.0 | 36.9% | 84.7% |
| Primary radiation .... | 40.6 | with correction for | with correction for |
| Total radiation ..... | 15.0 | accidental radiation | accidental radiation |
| Secondary radiation ... | 17.8 | and so forth | and so forth |
| Total radiation ..... | 14.4 | 28.5% | 83% |
| Primary radiation .... | 37.0 | | |
| Total radiation ..... | 14.0 | | |
| Secondary radiation ... | 16.4 | | |
| Total radiation ..... | 14.4 | | |

X-RAYS FILTERED WITH 1 MM. OF COPPER

| Method of measuring | 5 units of scale of electrometer in seconds | Primary radiation in % of total radiation | Secondary radiation in % of total radiation |
|---|---|---|---|
| Total radiation ..... | 24.0 | | |
| Primary radiation .... | 59.0 | | |
| Total radiation ..... | 23.8 | | |
| Secondary radiation ... | 28.2 | | |
| Total radiation ..... | 23.0 | 40.5% | 84.7% |
| Primary radiation .... | 57.0 | with correction for | with correction for |
| Total radiation ..... | 22.4 | accidental radiation | accidental radiation |
| Secondary radiation ... | 26.6 | and so forth | and so forth |
| Total radiation ..... | 21.2 | 31.5% | 82.5% |
| Primary radiation .... | 54.2 | | |
| Total radiation ..... | 22.8 | | |
| Secondary radiation ... | 26.4 | | |
| Total radiation ..... | 22.8 | | |

We see from these tabulations that the amount of the dose due to secondary radiation not only amounts to a considerable percentage of the total dose, but even surpasses the amount obtained from the primary radiation with the size of field chosen.

We did not use the Coolidge tube in these tests in the preceding ones, but a Lilienfeld tube. The reason is as follows: The source of radiation in the Coolidge tube is not solely to be sought for in the focus of the anticathode, for the entire anticathode with its metal arm emits radiations. This may be proven with a pin-hole camera. The presupposition for the determination of the absolute amount of secondary rays according to the described method is, as one may easily explain from geometrical considerations by means of Fig. 33, that the starting point of the X-rays on the anticathode is small, by no means larger than by 1 sq. cm. of the size of the diaphragm $B_1$, for if the starting point of the X-rays of the anticathode is greater than diaphragm $B_1$ then the diaphragm $B_1$ will not cut out all the direct rays from the measuring chamber, but part of the direct X-rays will strike the measuring chamber in an unfiltered state and the measured amount of secondary rays will appear to be too great. A similar deliberation will demonstrate that a slight error is also present in the determination of X-rays directly striking the measuring chamber. The experiments which we carried on with the Coolidge tube as radiation source confirmed this suspicion. If we added the doses measured for secondary rays to that for primary rays we did not obtain the sum value of the total dose, but the sum gave a value about 30 per cent too high.

*Influence of the Size of the Field on the Time Duration of Application of the Dose.*

The fact that secondary rays contribute a large share to the total dosage at a place within the area traversed by the rays, suggests the possibility that the size of the amount differs depending on the extent of the radiated surrounding water. The size of the field may not be without influence on the dose.

We have investigated the influence of the port of entry on the dose at the surface as well as in the depth. We have always measured the dose in the middle of the field, the focus being placed in a vertical axis of the center of the radiation field.

The details of the experiments were as follows: The X-ray tube R (see Fig. 34) contained in the bowl T, was placed at a focal distance (F. H.) of 30 cm. from the surface of the water in the phantom. Various sized diaphragms (B) could be inserted by means of a special holder on the surface of the water. In the center of the diaphragms a square was cut out, the sides (D) of which were of different sizes. The size of the field on the surface of the water was therefore determined by these openings. The sizes of fields were 4

| Size of field cm. | 5 units of scale of electrometer in seconds | Ratio of times of application |
|---|---|---|
| 4 × 4 | 41.6 | |
| 12 × 12 | 31.6 | |
| 4 × 4 | 39.2 | $\frac{39.9}{29.0}=1.35$ |
| 12 × 12 | 27.8 | |
| 4 × 4 | 39.0 | |
| 12 × 12 | 28.6 | |

The table shows that with X-rays filtered with 1 mm. copper a dependency of the time of application of a known dose from the size of the field is present. The dependency, as seen from Fig. 35, is more marked than with 3 mm. aluminum. This greater dependency is perhaps caused by the fact that the extent of the area from which the secondary radiation of the radiated water may enter the measuring chamber is much larger with the harder rays, filtered with 1 mm. copper. The following table gives the results of a test with X-rays filtered with 3 mm. aluminum, in which the measuring chamber was placed at a depth of 8 cm.

TIME OF APPLICATION OF X-RAYS FILTERED WITH 3 MM. OF ALUMINUM FOR VARIOUS SIZES OF FIELDS IN A DEPTH OF 8 CM.

| Size of field cm. | 5 units of scale of electrometer in seconds | Ratio of times of application |
|---|---|---|
| 4 × 4 | 33.8 | |
| 6 × 6 | 24.2 | |
| 4 × 4 | 33.2 | $\frac{33.0}{24.6}=1.34$ |
| 6 × 6 | 25.0 | |
| 4 × 4 | 32.0 | |
| 6 × 6 | 24.6 | |
| | | |
| 4 × 4 | 30.6 | |
| 8 × 8 | 21.6 | |
| 4 × 4 | 33.0 | $\frac{32.1}{21.0}=1.53$ |
| 8 × 8 | 21.0 | |
| 4 × 4 | 32.6 | |
| 8 × 8 | 20.4 | |
| | | |
| 4 × 4 | 34.4 | |
| 10 × 10 | 18.6 | |
| 4 × 4 | 32.4 | $\frac{32.3}{18.2}=1.78$ |
| 10 × 10 | 18.2 | |
| 4 × 4 | 30.0 | |
| 10 × 10 | 17.8 | |
| | | |
| 4 × 4 | 33.6 | |
| 12 × 12 | 16.0 | |
| 4 × 4 | 31.2 | $\frac{32.1}{16.4}=1.96$ |
| 12 × 12 | 16.2 | |
| 4 × 4 | 31.4 | |
| 12 × 12 | 17.0 | |

We conclude from the numerical values that in the depth also a dependence of the time of application from the size of the field is present. The dependence in the depth, as seen in Fig. 35, is much

more marked than on the surface, the time of application with a field of 4 by 4 cm. and with a field of 12 by 12 cm. are nearly in a ratio of 1 : 2.

The results of an analogous test with X-rays filtered with 1 mm. copper in a depth of 8 cm. are collected in the next table. Here also a much more pronounced dependence of the dose from the size of the field is obtained than on the surface.

TIME OF APPLICATION OF X-RAYS FILTERED WITH 1 MM. OF COPPER FOR FIELDS OF VARIOUS SIZES IN A DEPTH OF 8 CM.

| Size of field cm. | 5 units of scale of electrometer in seconds | Ratio of times of application |
|---|---|---|
| 4 × 4 | 117 | |
| 6 × 6 | 83 | |
| 4 × 4 | 112 | $\frac{113}{87}=1.30$ |
| 6 × 6 | 90 | |
| 4 × 4 | 111 | |
| 6 × 6 | 87 | |
| 4 × 4 | 114 | |
| 8 × 8 | 72 | |
| 4 × 4 | 119 | $\frac{116}{73}=1.59$ |
| 8 × 8 | 72 | |
| 4 × 4 | 116 | |
| 8 × 8 | 76 | |
| 4 × 4 | 115 | |
| 10 × 10 | 65 | |
| 4 × 4 | 118 | $\frac{116}{65}=1.78$ |
| 10 × 10 | 64 | |
| 4 × 4 | 116 | |
| 10 × 10 | 66 | |
| 4 × 4 | 112 | |
| 12 × 12 | 55 | $\frac{110}{57}=1.93$ |
| 4 × 4 | 109 | |
| 12 × 12 | 58 | |
| 4 × 4 | 109 | |
| 12 × 12 | 57 | |

A difference in the dependence of the time of application on the size of the field of x-rays filtered with 3 mm. aluminum and 1 mm. copper is not observable. (See Fig. 35.) The absence of the difference with the two qualities of rays in the depth in comparison to the surface may be explained by assuming that the rays filtered with 3 mm. aluminum have experienced an essential hardening after passing a layer of water 8 cm. thick, while the X-rays filtered with 1 mm. copper did not materially change in hardness after passing through 8 cm. of water. At the surface we have rays of a different hardness, which caused a difference in the range of action of the secondary rays, while in the depths the range of action of the secondary rays has been almost equalized by the adjustment in the difference of hardness of the rays.

In looking over the results of the tests the questions arise whether

the influence of the size of the field by a further increase of size would be equally noticeable, or whether beyond a certain size a further shortening in the time duration of application of a known dose will not take place. The answer to the questions is best given from the curves in Fig. 35. The course of the graphs is not a straight one, as should be expected if the influence of the size of the field on the time of the application would ascend uniformly, but the course of the graphs is a broken one in the sense that the influence of the size of the field gradually decreases with an increase in the size of the field. The graphs slowly approach a horizontal course, i.e., after

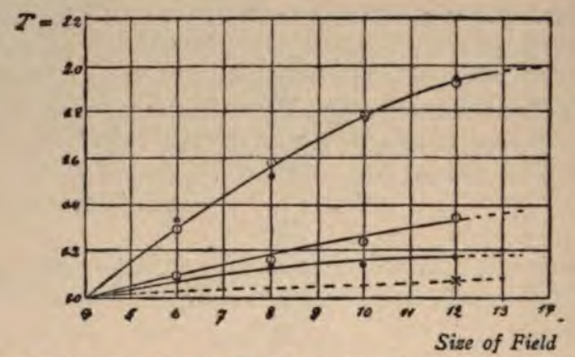



FIG. 35.—Influence of size of field on time of application of dose.

a certain size of field (about 20 cm.) is attained, a further increase in the size of the field does not assert any influence on the time duration of application of the dose in the center of the field. The result of the preceding investigation therefore is: *The size of the field has an important influence on the time duration of the application of the dose.*

*Significance of the Size of the Field for the Quotient of the Dose.*

From the marked dependence of the time duration of the application for a given dose on the size of the field in the depth in comparison to the surface, as we have shown in the preceding investigations, the conclusion must be drawn that the ratio of the depth dose to the surface dose, which in literature is designated as the quotient of dose, depends on the selection of the size of the port of entry. The great importance which the employment of a most favorable quotient of dose assumes in deep therapy induced us to make careful investigations. We again made use of the water phantom in these tests. Adhering to the details observed in our biologic observations, we chose a distance of focus from surface of 50 cm. and as varieties of sizes of field 5 by 5 cm., 10 by 10 cm. and 15 by 15 cm. The depths at which we carried out our investigations were 5 and 10 cm. The course of the experiment was altogether the same as in the preceding one. The filters chosen were 3 mm. aluminum, 10 mm. aluminum and 1 mm. copper.

After the constancy of the rays had been tested with a few control readings the time was alternately determined at the surface and the depth, within which the hand of the electrometer passed five units of the scale with a known size of the field. The size of the field was changed by the adjustable diaphragm located at the base of the tube bowl and the same measurements again executed. The following tables show three examples for a number of such tests for the three qualities of rays examined. In the first column the size of the field is stated, in the second the method of measuring is entered, the third column gives the time passed by the hand of the electrometer for five divisions of the scale in seconds, while in the last column the quotient of dose for the different sizes of fields is entered.

From the three tables we deduce the result: The quotient of the dose is very much dependent on the size of the field. It is the more favorable, the larger the field is. A larger quantity of X-rays, i.e., 19 per cent more, are applied in the depth of 5 cm. with a field size of 15 by 15 cm. than with a field size of 5 by 5 cm. with the same surface dose, while in a depth of 10 cm. the amount is even 36 per cent more in the larger field. With X-rays filtered with 10 mm. aluminum the difference found with fields of similar sizes in a depth of 5 cm. is 18 per cent, and of 10 cm. 29 per cent.

X-RAYS FILTERED WITH 3 MM. OF ALUMINUM

| Size of field cm. | Method of Measurement | 5 units of scale of electrometer in seconds | Quotient of dose |
|---|---|---|---|
| | 0 | 25.4 | |
| | 5 cm. depth | 64.8 | |
| 5 × 5 | 0 | 26.0 | 0.39 |
| | 5 cm. depth | 66.0 | |
| | 0 | 26.0 | |
| | 5 cm. depth | 66.2 | |
| | 0 | 21.8 | |
| | 5 cm. depth | 49.0 | |
| 10 × 10 | 0 | 22.2 | 0.44 |
| | 5 cm. depth | 49.6 | |
| | 0 | 21.8 | |
| | 5 cm. depth | 49.4 | |
| | 0 | 19.4 | |
| | 5 cm. depth | 41.0 | |
| 15 × 15 | 0 | 20.0 | 0.48 |
| | 5 cm. depth | 40.0 | |
| | 0 | 20.0 | |
| | 5 cm. depth | 41.0 | |
| | 0 | 27.8 | |
| | 10 cm. depth | 199.0 | |
| 5 × 5 | 0 | 26.2 | 0.14 |
| | 10 cm. depth | 192.0 | |
| | 0 | 27.2 | |
| | 10 cm. depth | 190.0 | |

| Size of field cm. | Method of Measuring | 5 units of scale of electrometer in seconds | Quotient of dose |
|---|---|---|---|
| | 0 | 21.8 | |
| | 10 cm. depth | 111.8 | |
| 10 × 10 | 0 | 22.0 | 0.20 |
| | 10 cm. depth | 110.8 | |
| | 0 | 21.8 | |
| | 10 cm. depth | 113.0 | |
| | 0 | 19.4 | |
| | 10 cm. depth | 90.4 | |
| 15 × 15 | 0 | 19.8 | 0.22 |
| | 10 cm. depth | 90.4 | |
| | 0 | 20.2 | |
| | 10 cm. depth | 89.4 | |
| | X-RAYS FILTERED WITH 10 MM. ALUMINUM | | |
| | 0 | 37.6 | |
| | 5 cm. depth | 79.0 | |
| 5 × 5 | 0 | 38.2 | 0.48 |
| | 5 cm. depth | 49.0 | |
| | 0 | 38.4 | |
| | 5 cm. depth | 82.0 | |
| | 0 | 34.0 | |
| | 5 cm. depth | 61.0 | |
| 10 × 10 | 0 | 31.4 | 0.55 |
| | 5 cm. depth | 58.4 | |
| | 0 | 32.4 | |
| | 5 cm. depth | 58.6 | |
| | 0 | 30.0 | |
| | 5 cm. depth | 50.0 | |
| 15 × 15 | 0 | 29.4 | 0.59 |
| | 5 cm. depth | 49.8 | |
| | 1 | 29.2 | |
| | 5 cm. depth | 50.4 | |
| | 0 | 42.2 | |
| | 10 cm. depth | 191.0 | |
| 5 × 5 | 0 | 40.0 | 0.22 |
| | 10 cm. depth | 190.0 | |
| | 0 | 40.4 | |
| | 10 cm. depth | 188.0 | |
| | 0 | 33.2 | |
| | 10 cm. depth | 121.0 | |
| 10 × 10 | 0 | 33.0 | 0.27 |
| | 10 cm. depth | 119.0 | |
| | 0 | 31.4 | |
| | 10 cm. depth | 120.0 | |
| | 0 | 29.8 | |
| | 10 cm. depth | 93.0 | |
| 15 × 15 | 0 | 29.9 | 0.31 |
| | 10 cm. depth | 96.0 | |
| | 0 | 29.0 | |
| | 10 cm. depth | 96.0 | |

X-RAYS FILTERED WITH 1 MM. COPPER

| Size of field cm. | Method of Measuring | 5 units of scale of electrometer in seconds | Quotient of dose |
|---|---|---|---|
| | 0 | 63.0 | |
| | 5 cm. depth | 113.0 | |
| 5 × 5 | 0 | 61.0 | 0.56 |
| | 5 cm. depth | 110.0 | |
| | 0 | 63.4 | |
| | 5 cm. depth | 111.0 | |
| | 0 | 50.2 | |
| | 5 cm. depth | 80.0 | |
| 10 × 10 | 0 | 52.2 | 0.64 |
| | 5 cm. depth | 80.0 | |
| | 0 | 51.8 | |
| | 5 cm. depth | 79.0 | |
| | 0 | 49.6 | |
| | 5 cm. depth | 68.0 | |
| 15 × 15 | 0 | 47.8 | 0.73 |
| | 5 cm. depth | 66.0 | |
| | 0 | 46.6 | |
| | 5 cm. depth | 64.0 | |
| | 0 | 62.4 | |
| | 10 cm. depth | 205.0 | |
| 5 × 5 | 0 | 66.0 | 0.31 |
| | 10 cm. depth | 209.0 | |
| | 0 | 67.4 | |
| | 10 cm. depth | 211.0 | |
| | 0 | 57.4 | |
| | 10 cm. depth | 151.0 | |
| 10 × 10 | 0 | 57.2 | 0.38 |
| | 10 cm. depth | 150.0 | |
| | 0 | 58.2 | |
| | 10 cm. depth | 149.0 | |
| | 0 | 54.2 | |
| | 10 cm. depth | 122.0 | |
| 15 × 15 | 0 | 52.8 | 0.43 |
| | 10 cm. depth | 124.0 | |
| | 0 | 52.4 | |
| | 10 cm. depth | 125.0 | |

X-rays filtered with 1 mm. copper give, with an otherwise like surface dose, with a field size of 15 by 15 cm. a dose 23 per cent higher than with a field of 5 by 5 cm. The difference in the depth doses at a depth of 10 cm. with the two field sizes is 28 per cent. If we compare the values obtained from the various radiations with each other, we find with the exception of the field 5 by 5 cm. and of X-rays filtered with copper and 5 cm. depth, that the dependence of the quotient of dose on the size of field is much more marked with the soft rays, and that therefore the quotient of dose is more favorable in larger field sizes in comparison to smaller fields if a softer radiation is used. The tests described in the previous chapter on the

dependence of the size of application of the given dose on the size of field conforms to these results.

Here also a further increase in the size of field beyond a certain size is finally without any influence on the magnitude of the quotient of the dose. To express this in a graphic form, we refer to Fig. 36, in which the quotients of the doses have been plotted for a depth of 10 cm. for the three measured field sizes and for the three hardnesses investigated. Though only three points are at our disposal, we see that the course of the graphs is not a straight one, but gradually approaches a horizontal line with the larger fields.

If we ask why beyond a certain field size an influence of the field on the time duration of the application of the dose and on the quotient of the dose is not any more recognizable we may explain the fact as follows: If X-rays (as in Fig. 34) enter the water phantom through the larger field D, all of the water penetrated by the rays

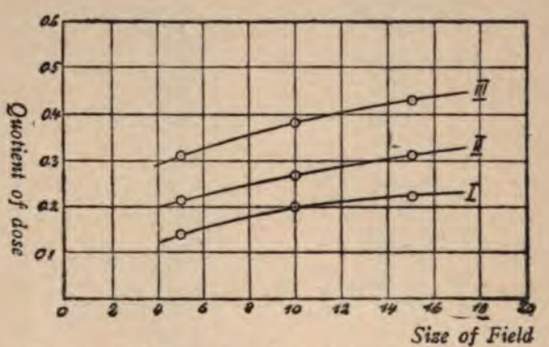



FIG. 36.—Relation of quotient of dose to size of field.

will send out secondary rays. The secondary rays also will strike the measuring chamber of the dosimeter, which is located in the center of the beam in the water. The regions of water directly surrounding the chamber permit the secondary rays to strike the chamber in an almost unweakened condition, and the farther the regions of the water, sending out secondary rays, are distant from the chamber, the much more are the secondary rays weakened by the greater distance and by the layer of water intervening between these regions and the measuring chamber. Finally, a distance from the measuring chamber K exists in which the secondary rays are so weakened that they do not any more possess an appreciable influence on the dose measured with the chamber. A certain region of the irradiated water around the measuring chamber therefore exists, the secondary rays of which contribute to the dose. The region is the more extensive, the harder, and therefore the more penetrating the rays are.

As long as in our experiments, on the dependence of the time of application on the size of field and on the dependence of the dose quotient on the field size, the field sizes investigated are lying within the range of these secondary rays, a dependence of the time duration

of the application and the quotient of the dose from the size of the field must be present. As soon as the field became larger than the length of the secondary radiations, a dependence of the time duration of the application on the quotient of the dose from the size of field will no longer exist, because the secondary rays arising within the region beyond that of the actually active secondary rays do not possess any more influence on the dose.

*Concerning the Influence of the Secondary Radiation on the Distribution of the Dose within and without the Radiated Region.*

We observed in the previous chapter what a great influence secondary rays have on the dose, what a large percentage of the dose at a place within the irradiated water is derived from secondary rays. The investigations showed that if the dose was measured in the center of the radiation field not all of the secondary radiations of the peripheral portions of the field contributed to the dose, but the farther distant the regions emitting secondary rays are from the center of the field, the smaller a portion of its secondary rays reaches the center of the field. We spoke of a distinct limitation of the action of the secondary rays.

The conclusion may be drawn from the results that the dose is not of an equal size in all the regions of the radiation field. The dose will be largest in the middle of the field and gradually decrease towards the periphery. All of the irradiated water in the center influences the dose, while at the periphery of the field only a part is active.

Another conclusion which may be drawn from the results of the previous chapter is that the regions of water surrounding the radiation field proper will receive a certain dose during radiation derived from the secondary rays of the radiation field. The region of water to which, through a field of known size, a dose of X-rays is to be given, will not be a sharply limited one, but the surrounding parts also will receive a certain X-ray dose. The transition of the intensity of rays from the radiation field proper to the surrounding part which will not receive any radiations, also will be a gradual one.

To subject these conclusions to an experimental test the following method was used, which is schematically represented in Fig. 37. We used as water phantom a large glass trough, Tr. The chamber K was introduced to the center of the trough through a glass tube which was densely packed with wax to prevent the entrance of water. The surface of the water was 8 cm. above the chamber. The anticathode of the X-ray tube R, which was placed in a bowl T, was located at a distance, FH, of 50 cm. from the surface of the water. The bowl was carried by the stand S, the horizontal arm of which was movable and provided with a scale Sk, divided in centimeters. The diaphragm B made from heavy lead sheeting served to limit the field. The diaphragm B was rigidly fixed to the bowl with a connecting rod V. If

the X-ray tube was moved by moving the horizontal arm then diaphragm B would simultaneously move. The diaphragm B rested on a sliding arrangement, Sch, made from wood, to facilitate the horizontal motion of the X-ray tube and diaphragm. The measurement of the dose at various places within the field was attained by the moving of the X-ray tube and radiation field, while the measuring chamber K remained stationary. The filter F — for these tests we used X-rays filtered with 1 mm. copper—was placed closely beneath the bowl.

The course of the experiment closely adhered to those observed in the preceding investigations. The constancy of the source of radiation was ascertained by a few control measurements. The time was always observed within which the electrometer passed through five divisions of the scale. Starting with the position of the anticathode directly above the measuring chamber K, the X-ray with

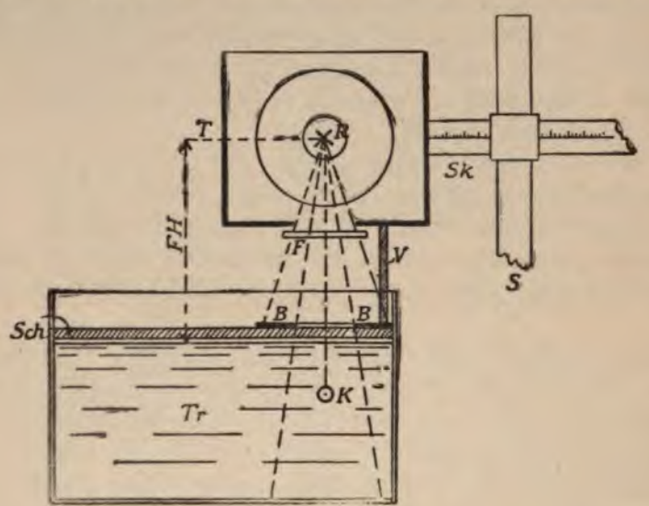



Fig. 37.

the diaphragm was moved laterally from centimeter to centimeter and the electrometer read each time. Between every one of these readings a control measurement was inserted with a vertical position of the focus above the measuring chamber. The results of the measurements of a few series of these experiments are entered in the following tables. In the first column is the method of measuring, i.e., the position of the X-ray and diaphragm in reference to the measuring chamber; in the second column the reading times of the electrometer are entered in seconds; while in the fourth column the calculated dose in per cent of the dose measured in the center of field, i.e., the vertical position of the anticathode above the measuring chamber.

The first table shows the results of measuring with a field the size of 4 by 4 cm. Fig. 38 represents the graph of these results.

X-RAYS FILTERED WITH 1 MM. OF COPPER
SIZE OF FIELD, 4 SQ. CM.

| Method of measuring | Time consumed to register 5 units of scale of electrometer in seconds | Time consumed to register 5 units of scale of electrometer in seconds with correction | Dose in % of dose measured in center of radiation field |
|---|---|---|---|
| 0 cm. | 33.8 | 33.8 | 100 |
| 1 " | 33.0 | 33.0 | 101 |
| 0 " | 32.8 | 32.8 | — |
| 2 " | 35.4 | 35.4 | 94 |
| 0 " | 33.8 | 33.8 | — |
| 3 " | 91.0 | 95.0 | 35 |
| 0 " | 34.0 | 34.0 | — |
| 4 " | 140.0 | 146.0 | 23 |
| 0 " | 33.4 | 33.4 | — |
| 6 " | 262.0 | 287.0 | 12 |
| 0 " | 35.6 | 35.6 | — |
| 8 " | 428.0 | 520.0 | 6.5 |
| 0 " | 33.4 | 33.4 | — |
| 10 " | 522.0 | 655.0 | 5 |
| 0 " | 34.8 | 34.8 | — |
| 15 " | 701.0 | 920.0 | 3.8 |
| 0 " | 34.8 | 34.8 | — |

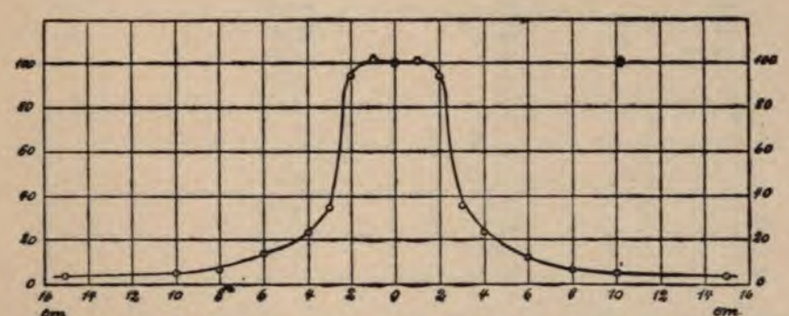



FIG. 38.—Influence of secondary radiation on the distribution of dose within and without the radiation field of 4 sq. cm., measured in water phantom.

From table and figure we see that the dose does not drop suddenly to zero with the geometrical limits of the field of radiation, but that a gradual decrease of the dose takes place with an increase in distance from the radiation field. Within a distance of 2 cm. measured outward from the geometrical limit of the radiation field, a little more than 20 per cent of the dose applied by the central beam still exists, and at a distance of 6 cm. from the limit of the radiation field a markedly smaller dose is still recognizable.

The next table shows an analogous measurement with a field size of 8 by 8 cm., while Fig. 39 represents the graph plotted from this value.

X-RAYS FILTERED WITH 1 MM. OF COPPER
SIZE OF FIELD, 8 SQ. CM.

| Method of measuring | Time consumed to register 5 units of scale of electrometer in seconds | Time consumed to register 5 units of scale of electrometer in seconds with correction | Dose in % of dose measured in center of radiation field |
|---|---|---|---|
| 0 cm. | 21.0 | 21.0 | 100 |
| 1 " | 21.4 | 21.4 | 100.5 |
| 0 " | 22.0 | 22.0 | — |
| 2 " | 23.0 | 23.0 | 96 |
| 0 " | 22.0 | 22.0 | — |
| 3 " | 25.0 | 25.0 | 94 |
| 0 " | 25.0 | 25.0 | — |
| 4 " | 30.6 | 30.6 | 81 |
| 0 " | 24.6 | 24.6 | — |
| 5 " | 41.0 | 41.8 | 58 |
| 0 " | 24.0 | 24.0 | — |
| 6 " | 68.0 | 69.4 | 36 |
| 0 " | 26.0 | 26.0 | — |
| 7 " | 102.0 | 106.0 | 23.6 |
| 0 " | 24.0 | 24.0 | — |
| 9 " | 196.0 | 208.0 | 12.7 |
| 0 " | 24.6 | 24.6 | — |
| 12 " | 339.0 | 385.0 | 6.4 |
| 0 " | 24.4 | 24.4 | — |
| 15 " | 512.0 | 622.0 | 0 |
| 0 " | 25.2 | 25.2 | — |

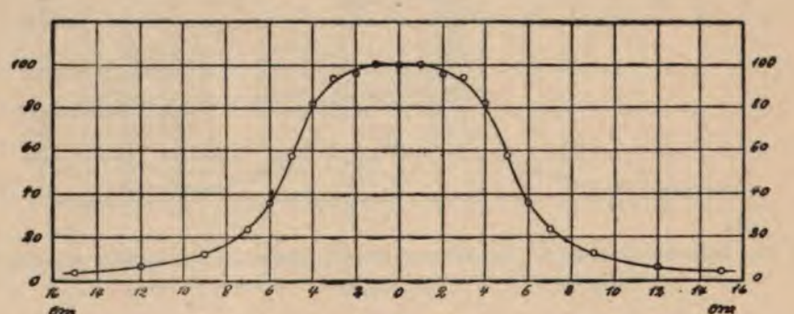



FIG. 39.—Influence of secondary radiation on the distribution of dose within and without the radiation field of 8 sq. cm. measured in the water phantom.

From the table and graph we deduce that here also a sharp limitation of the field of radiation is not present, but that in a distance of 2 cm. beyond the geometrical limits of the field a noticeable radiation dose may still be ascertained. It amounts with this field size at a distance of 2 cm. beyond the periphery of the field to almost 20 per cent, and at a distance of 6 cm. to 10 per cent of the dose applied by the central beam. We also see from the measuring that the distribution within the radiation field is not uniform, but that within a known time duration of radiation the dose is largest in the center of the radiation field and gradually decreases towards the periphery. This was to be expected according to the investigations on the influ-

ence of secondary radiations. The difference of the dose in the center of the field and of that at the periphery for a field size of 8 by 8 cm. amounts to about 20 per cent.

In the next table the results of an analogous measurement with a field size of 12 by 12 cm. are entered. Fig. 40 represents the results in a graph.

X-RAYS FILTERED WITH 1 MM. OF COPPER
SIZE OF FIELD, 12 SQ. CM.

| Method of measuring | Time consumed to register 5 units of scale of electrometer expressed in seconds | Time consumed to register 5 units of scale of electrometer expressed in seconds with corrections | Dose in % of dose measured in center of field |
|---|---|---|---|
| 0 cm. | 17.0 | 17.0 | 100 |
| 1 " | 16.8 | 16.8 | 100 |
| 0 " | 16.6 | 16.6 | — |
| 2 " | 16.8 | 16.8 | 99 |
| 0 " | 16.6 | 16.6 | — |
| 3 " | 18.2 | 18.2 | 95 |
| 0 " | 18.0 | 18.0 | — |
| 4 " | 19.6 | 19.6 | 89 |
| 0 " | 16.8 | 16.8 | — |
| 5 " | 19.4 | 19.4 | 88 |
| 0 " | 17.2 | 17.2 | — |
| 6 " | 21.8 | 21.8 | 78.5 |
| 0 " | 17.0 | 17.0 | — |
| 7 " | 26.0 | 26.0 | 65.5 |
| 0 " | 17.0 | 17.0 | — |
| 8 " | 42.0 | 42.0 | 40.5 |
| 0 " | 17.0 | 17.0 | — |
| 10 " | 82.0 | 84.0 | 19.5 |
| 0 " | 16.0 | 16.0 | — |
| 12 " | 120.0 | 125.0 | 12.8 |
| 0 " | 16.0 | 16.0 | — |
| 15 " | 235.0 | 265.0 | 6.3 |
| 0 " | 17.2 | 17.2 | — |

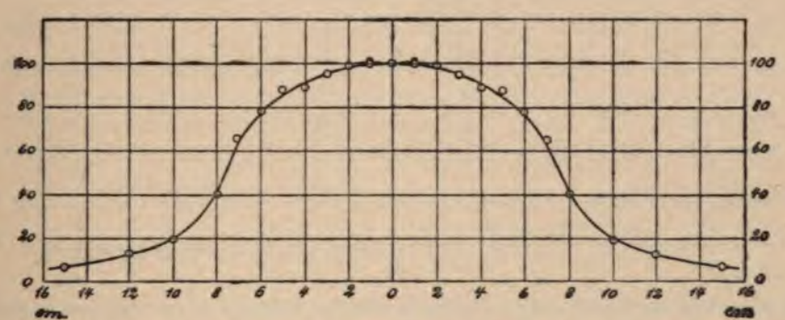



FIG. 40.—Influence of secondary radiation on the distribution of dose within and without the radiation field of 12 sq. cm. measured in the water phantom.

From the table and graph we see that here also the influence of secondary radiations on the distribution of the dose within and without the radiation field is noticeable to a marked degree. The decrease of the dose with an increasing distance from the radiation field is

here still more gradual than in the series of experiments with the smaller field sizes.

In order to demonstrate that the results given in these series of measurements are really caused by the secondary rays emitted from the irradiated water of the phantom, we add another series of measurements which was obtained by the same methods of experimentation, however, with the difference that the water was removed from the phantom; therefore the secondary rays arising in the air and also in the bottom of the phantom only could exert an influence. The measurements were made in a field of 5 by 5 cm. The measurements are given in the following table and the graph in Fig. 41.

X-RAYS FILTERED WITH 1 MM. OF COPPER
SIZE OF FIELD, 5 SQ. CM.

| Method of measuring | Time consumed to register 5 units of scale of electrometer in seconds | Time consumed to register 5 units of scale of electrometer in seconds with correction | Dose in % of dose measured in center of field |
|---|---|---|---|
| 0 cm. | 50.0 | — | 100 |
| 1 " | 49.5 | 52.0 | 102 |
| 0 " | 49.5 | — | — |
| 2 " | 52.0 | 55.0 | 100 |
| 0 " | 54.0 | — | — |
| 3 " | 61.0 | 65.0 | 89 |
| 0 " | 56.0 | — | — |
| 4 " | 385.0 | 620.0 | 10 |
| 0 " | 58.0 | — | — |
| 5 " | 840.0 | 2200.0 | 3 |
| 0 " | 65.0 | — | — |
| 10 " | 810.0 | 2130.0 | 3.2 |
| 0 " | 62.0 | — | — |

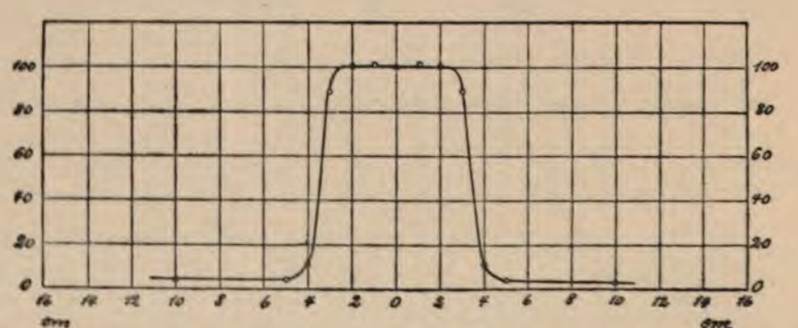


FIG. 41.—Influence of secondary radiation on the distribution of dose within and without the radiation field of 5 sq. cm. measured in the empty water phantom.

From the table and graph we see that the limits of the field of radiation are much more clearly defined than in the investigations made with the phantom filled with water. The dose has already depreciated to an amount scarcely measurable within a distance of 2 cm. from the geometrical limits of the radiation field. This result

was to be expected on account of the much smaller secondary radiation from the air in comparison to that of water.

The results of the experiments described in this chapter may be summarized in the following sentences:

1. *Secondary radiation exercises an important influence on the distribution of the dose within and without the radiation field.*

2. *The dose is largest in the center and decreases gradually towards the periphery of the radiation field.*

3. *The limitation of the field of radiation is not clearly defined but a gradual decrease of the dose occurs with an increase in distance outwardly from the periphery of the radiation field.*

Though these experiments were performed only with X-rays filtered with 1 mm. copper, one must conclude from the results of the other investigations on secondary rays, that with the use of other qualities of rays a similar influence of the secondary rays on the distribution of the dose within and without the radiation field exists.

## PART II.

# THE BIOLOGIC PRINCIPLES OF RADIATION THERAPY

In the first part of the book we saw that it is possible with physical measuring methods to gain an opinion on the quality of the rays employed and on the size of the dose applied. We have mentioned as a practical measuring method the ionization method and specified an instrument of practical usefulness.

With the aid of these measuring methods we have attempted to define the laws which govern the action of the X-rays and rays of radioactive substances on biologic objects.

It appeared to be of special importance to ascertain whether laws may be propounded for the following questions which are of practical importance in deep therapy:

I. Is with the same dose the degree of the biologic action of X- and gamma-rays dependable on the hardness?

II. Is with the same dose the degree of biologic action the same if the dose is applied with a great intensity of rays within a short time or with a small intensity of rays within a long time? (Schwarzschild's law.)

III. Is with the same dose the intensity of the biologic action the same if the dose is applied in one sitting or in fractional doses with definite time intervals? (Law of the intermittent dose.)

IV. With the same dose, is the intensity of the biologic action influenced by factors as secondary radiation, diathermy, heat, etc.?

We realized from the start that these laws could not be promulgated without other additional investigations being made first. Conditions are so extremely complicated in such differentiated organisms as the human body. Therefore we first had to attempt to determine the laws in animals and vegetable organisms of a lower order and then investigate whether they could be applied to the human body.

### Experiments on the Usefulness of Frog Larvæ as Test Objects

A biologic object is useful for our purposes as test object:

1. If it reacts to an applied dose of X- or gamma-rays with characteristic and easily recognizable changes in form and function;

2. If these characteristic changes are already noticeable in varying degrees with relatively small differences in the dose, that is, if the test object is sufficiently sensitive;

3. If the biologic object may be easily procured in such great

numbers of the same origin that the result of the experiments is not influenced by individual differences.

We have tested the most varied biologic objects for these requirements, and have finally and almost exclusively employed the larvæ of frogs, as had already been done by Gauss and Lembke.

A female frog of rana temporaria or rana esculenta lays her spawn in a big ball-like clump in stagnant water. A short time after the expulsion from the womb the eggs of rana temporaria swell in the water to a size of a diameter of about 1 cm. The eggs of rana esculenta are somewhat smaller. The spawn of the frogs, L (see Fig. 42), was placed on a stand made of thin glass rods which enclosed a circular area 1 cm. high and 8 cm. in diameter, the floor and walls

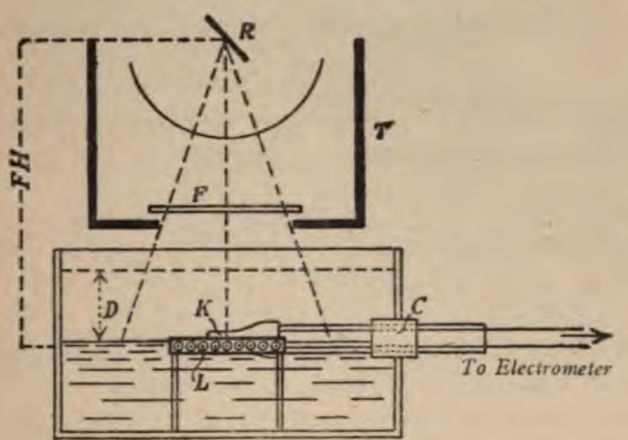



FIG. 42.

of which were made of thin gauze. Thus the radiation dose could be applied to all the eggs at the same time. The eggs were placed within this limited space in one layer corresponding to their size. The ionization chamber K, serving to measure the dose, was placed next to the stand at the same height as the layer of frogs L in such a manner that at a certain place C a glass tube was sealed in, which was closed with a thin rubber cap for the reception of the ionization chamber. The ionization chamber in all these experiments with larvæ consisted of a cylindrical, very thin walled (0.1 mm.) aluminum chamber, described more in detail in Part I. We will later discuss in how far the results of measurements with such an aluminum chamber must be corrected in the quantitative determination of the dependence of the intensity of the biologic action on the hardness of the rays.

The radiation was always performed in pond water. The vessel used for the experiments was of glass of a diameter of 25 cm. and a height of 12 cm., which was filled with pond water up to 6 cm., that is, to such a height that the frog spawn was just covered with

water. We will see later why we thought it correct to use such a large vessel for our experiments.

A Coolidge tube was used almost exclusively as a source of radiation for X-rays because it is constant and easily controlled during its operation. It was placed in a tube stand which could be easily moved in all directions and was provided with a bowl of leaded glass. Beneath the tube bowl (T) exchangeable diaphragms and the filter (F) could be placed. An inductor with gas interruptor was exclusively used for the tests in these experiments on frogs' spawn. The focus of the X-rays (R) was vertically above the center of the glass bowl, and at such a focal distance (FH) from it that the decrease of the intensity of the X-rays within the radiation field could be neg-

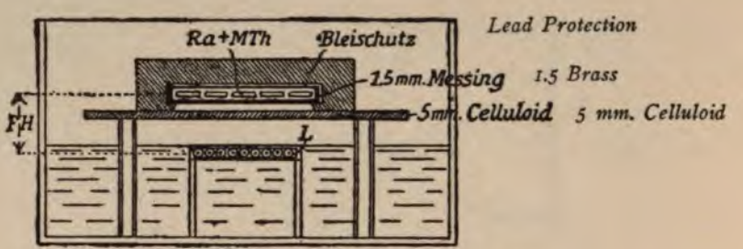



FIG. 43.

lected. Thereby we attained that all of the frog's spawn received the same dose measured with the ionization chamber.

The radium cannon, described in Part I, in which the radium served as source of radiation from radioactive substances and mesothorium preparations, was mounted as evenly as possible upon a circular layer of a diameter of 10 cm. The rays were filtered with 1.5 mm. brass and 5 mm. celluloid. (See Fig. 43.)

The cannon was kept at a distance (FH) of 4 cm. from the frog spawn in the glass trough by three glass supports. The measurement of the dose for the radiation with gamma-rays of radium and mesothorium was performed in the following manner:

The ionization chamber was first placed where later the middle of the frog larvæ would be. The time was determined within which the dose would be attained at this place. The ionization chamber was then removed and the stand with the frog larvæ inserted, the conditions remaining otherwise the same. As we possessed a constant source of radiation in radium and mesothorium, the time within which the desired dose was obtained could be calculated by comparison from the time within which a unit of dose was measured with the iontometer.

We wish to mention that all metal parts must be carefully avoided within the glass trough because uncontrollable influences in the development of the test animals might result therefrom due to undesirable radiations.

With this arrangement of the experiment we next examined the usefulness of the frog larvæ as test objects.

*Characteristic Changes in Form and Function of Frog Larvæ after the application of a Dose of X- and Gamma-Rays.*

V. Hertwig had already drawn attention to the characteristic changes observed in his experiments by the action of radium in young frog eggs which appear during the progress of the period of development of the eggs to young larvæ. They consist essentially in deformities of the larvæ which are marked by curvatures and blister

FIG. 44.—Normal development of larvæ of frog.

formations mostly on the belly (abdominal dropsy). Hertwig designated these symptoms as radiation or radium sickness of the frog larvæ, which designation we also will employ.

We subjected the experiments of V. Hertwig to control examinations and confirmed and extended them further to X-rays. We saw that the same deformities of the frog larvæ also appeared following radiation with X-rays and reproduce a few photographs which show larvæ of normal development and larvæ of abnormal development due to the radiation sickness produced by radiation.*

The frog larvæ continue to develop for some time in spite of the deformity and, finally, after a certain time interval succumb to the radiation disease.

We have always measured the dose in these control examinations according to the directions given above, and were enabled to determine that a most favorable dose for the repetition of these character-

* The photographs were obtained in the following manner: On the days of observation a few animals, which evinced a mean average of radiation symptoms, were taken from the culture plates and placed in diluted solution of formol for the purpose of preservation. The animals were photographed in water on a glass plate, divided in millimeters with a microphotograph. The divisions on the photograms give also a measure for the actual size of the animals.

istic changes exists. The symptoms of radium sickness are hardly noticeable with a small dose. The larvæ rapidly succumb if the dose is too great, due to the action of the radiation, without any characteristic changes having developed.

The experiments demonstrated further that the more youthful the frog larvæ are the more characteristic the development of the symptoms of radiation sickness will be. If the frog larvæ have already so far developed at the time of radiation that they have escaped from the membranes and swim about in the pond water, then they show the symptoms of the radiation sickness in a less marked degree, and often perish without any development of the symptoms.

We have made systematic investigations to prove the dependence of the formation of the characteristic symptoms of radiation sickness

FIG. 45.—Abnormal development of larvæ of frog under the influence of X-rays res. radium rays.

on the age of the frog larvæ with the same intensity of dose. The result of one of the four tests is reported in the following paragraph. The after tests also gave the same results with hardly any differences being observable.

*Method of Experiment.*—A large clump of spawn from a pair of rana temporaria served as test material for the radiation experiment. The date of delivery (March 20) was exactly known by continued observations of the female.

The clump of spawn was divided into eight almost even sized parts, each containing 100 eggs. Seven of these were exposed to radiations while one of the spawn clumps was kept as control in the same room in a glass trough of the same size as those used for the radiated groups. We radiated the seven spawn clumps at the same time of the day within a time interval of two days between each group beginning the first day after birth. We applied X-rays. At the time of radiation of the first group the indications of the first cleavage of the eggs was recognizable with a magnifying lens; at the

time of radiation of the last group the larvæ had already escaped from the oval membranes.

A large Coolidge tube was used in these experiments. It was operated with an inductor and gas interrupter, so that the potential energy at the tube corresponded to a parallel spark gap of 35 cm. An auxiliary spark gap of 5 cm. was also placed in series with the tube. The distance of the focus from the frog spawn was 35 cm. The dose was always 100 e. The rays were filtered with 10 mm. aluminum.

After radiation the radiated frog eggs were kept in pond water in large glass troughs like the controls. The pond water was replaced daily with fresh pond water. The larvæ were fed with the algæ attached to the water plants and later with steamed salad.

The excerpts from the observation journal are compiled in the following table.

THE DEPENDENCY OF SYMPTOMS PRODUCED WITH RADIATIONS

| | March 21 | March 23 | March 25 |
|---|---|---|---|
| Stage of development at commencement of observations. | Larvæ first day post-partum: 1-4 cell stage. | Four cell stage. | Larvæ are just assuming form within the oval membranes. |
| Observations six days after radiation. | The controls are so far developed that the larvæ have assumed form within the membranes, so that the head may be recognized from the rest of the body. | The controls are so far developed that head and tail end are visible within the membranes, but they do not as yet exhibit motion. | The controls are so far developed that they begin to show life. |
| | The radiated animals show a difference from the controls, as they are behind in development, have partly died and undergone decomposition. | The radiated animals already partly exhibit the characteristic deformity, the radium disease (curvature). | The radiated animals do not yet evince observable differences from the controls. |
| Observations eight days after radiation. | The controls are so far developed that head and tail ends are visible within the membranes, but do not as yet execute any movements. | The controls are so far developed that they already move within the membranes. | The controls have left the membranes and swim freely about in the hatching bowl. |
| | The radiated animals show distinct differences from the controls; the larger number are dead within the oval sac, while the rest present cloddy larvæ, | The characteristic curvature is even more characteristic; formation of blisters has not as yet occurred. | All radiated animals distinctly show formation of blisters and curvature (abdominal dropsy). |
| Observations ten days after radiation. | The controls have so far developed that they already execute movements within the oval membranes. | The controls have left the sac and swim about in the hatching bowl. | The larvæ are further developed and are on an average 1 cm. long. |
| | The radiated animals have not any further developed than March 29, but most of them have died. | All larvæ have the characteristic signs of abdominal dropsy. | The formation of blisters is plainly seen in the radiated animals. However, the larvæ have grown still further. |
| Observations twelve days after radiation. | The controls have left the sac and swim freely in the hatching bowl. | The larvæ are still further developed and measure on an average 1 cm. | The larvæ show normal development and are 1 cm. long. Trunk and tail end are plainly differentiated. |

OF LIKE DOSES ON THE AGE OF THE LARVÆ OF FROGS

| March 27 | March 29 | March 31 | April 2 |
|---|---|---|---|
| Larvæ within the oval membranes are somewhat farther advanced in development. | Larvæ are still within the membranes. Head and tail end visible. | Larvæ are still within the membranes, but show distinct movements. | Larvæ have escaped from the membranes. They swim freely within the hatching bowl. |
| The controls have left the membranes and swim freely about in the hatching bowl. | The larvæ are on an average 1 cm. long. | The controls show normal development. Larvæ are 1 cm. long. Trunk and tail end are plainly visible. | The controls are 11 mm. long and have grown somewhat stronger. |
| The radiated animals have also escaped from the membranes; however, most of them show the characteristic curvature and blisters of the radium disease. | The radiated animals do not show any anatomical differences from the controls. | The radiated animals do not show any differences from the controls. | The radiated animals do not show any distinctly visible differences from the controls. |
| The controls are more advanced in development and are 1 cm. long. | The controls show normal development. The larvæ are 1 cm. long. Trunk and tail end are plainly differentiated. | The controls are 11 mm. long and have grown somewhat stronger. | The controls have further advanced in normal development, grown stronger and are 11 mm. long. |
| Almost all of the radiated animals have abdominal dropsy. | The radiated animals do not show any essential differences from the unradiated controls. | The radiated animals do not show any essential differences from the unradiated controls. | The radiated animals do not show any visible differences from the controls. |
| The controls show normal development; larvæ are 1 cm. long. Trunk and tail end are plainly differentiated. | The controls are 11 mm. long and are somewhat stronger. | The controls continue to normally develop, have grown somewhat stronger, but are still 11 mm. long. | Trunk and tail end are plainly separated. Larvæ have grown stronger and are about 12 mm. long. |
| Symptoms of abdominal dropsy are not any more distinct; on the other hand, the larvæ are more deformed. | The radiated animals do not show any essential differences from the controls. | The radiated animals do not show any marked differences from the controls. | The radiated animals do not evince any marked difference from the controls. |
| The controls are 11 mm. long and have grown stronger. | The controls have continued to further develop normally and are about 11 mm. long. | Trunk and tail are clearly separated. The larvæ have grown stronger and are about 12 mm. long. | Trunk and tail are distinctly separated; the larvæ have grown still stronger; length somewhat above 12 mm. |

| | March 21 | March 23 | March 25 |
|---|---|---|---|
| Stage of development at commencement of observations. | Larvæ first day post-partum: 1-4 cell stage. | Four cell stage | Larvæ are just assuming form within the oval membranes. |
| | The radiated animals have not developed any more since March 31, and all have died. | The larvæ have grown somewhat more. The blisters occupy all of the region of the belly. | The larvæ have large blisters and are more curved. |
| Observations 14 days after radiation. | | The controls show normal development, are 1 cm. long; trunk and tail end are clearly differentiated. | The controls are 11 mm. long, and have grown somewhat stronger. |
| | | The larvæ have hardly grown in length. The formation of blisters is still more pronounced. The larvæ begin to die in more or less large numbers. They all died the next day. | The larvæ have large blisters and have grown slightly. |
| Observations 16 days after radiation. | | | The controls have continued in normal development and are about 11 mm. long. |
| | | | The radiated larvæ have not grown any further; the blisters develop to enormous size. The greater number has died. |
| Observations 18 days after radiation. | | | The controls show a plain separation of trunk and tail. The larvæ have grown larger; length about 12 mm. |
| | | | The larvæ, with the exception of a few, are all dead. |
| | | | The larvæ still living on April 14 have died. |

| March 27 | March 29 | March 31 | April 2 |
|---|---|---|---|
| Larvæ within the oval membranes are somewhat farther advanced in development. | Larvæ are still within the membranes. Head and tail end visible. | Larvæ are still within the membranes, but show distinct movements. | Larvæ have escaped from the membranes. They swim freely within the hatching bowl. |
| Signs of abdominal dropsy are seen in a few larvæ. The others show marked curvature. | The radiated animals do not show any signs of abdominal dropsy. On the other hand, a few show minute blister formation at the head. | The radiated animals do not show any essential differences from the controls. | The radiated animals do not show any essential differences from the controls. |
| The controls have further continued to normally develop and are about 11 mm. long. | The trunk and tail end are clearly defined. The larvæ have grown some stronger and are about 12 mm. long. | The trunk and tail end are clearly defined. The larvæ are somewhat stronger and somewhat longer than 12 mm. | Trunk and tail end are clearly defined. The caudal fin is already well formed. Head is the size of a lentil, length about 14 mm. |
| The greater number of larvæ have plainly distinct signs of abdominal dropsy and at the same time small blisters on the head. | Signs of abdominal dropsy are not yet seen in the radiated animals. Formation of minutest blisters on the head of some of the larvæ. The animals have remained plainly behind in length and size in comparison to the control animals. | The radiated animals do not show any essential differences in form compared to the controls. On the other hand, they have remained behind in growth, in length as well as circumference, in comparison with the controls. | In comparison to the controls, arrest in growth only is recognizable. |
| Trunk and tail end are clearly defined. The larvæ have grown larger and are about 12 mm. long. | Trunk and tail end are clearly defined. Larvæ have grown still larger. Length somewhat over 12 mm. | Head and trunk are distinctly differentiated; caudal fin well formed; head about size of lentil, length 14 mm. | Larvæ's head about size of lentil. Length about 14 mm. |
| The greater number of the radiated larvæ have signs of abdominal dropsy and blister formation on head. They have hardly grown any further. | The same findings as 14 days after radiation. | Findings exactly as 14 days after radiation. | The radiated animals show a slight retardation of growth compared to the controls. |
| Trunk and tail are distinctly defined. The larvæ have grown somewhat in size and are somewhat more than 12 mm. long. | Head and trunk are distinctly differentiated. Caudal fin already well developed. Head about size of lentil; length of larvæ about 14 mm. | The head is size of lentil; length about 14 mm. | The larvæ have hardly perceptibly grown since April 18. |
| The greater number of larvæ have died. Part of the survivors show signs of abdominal dropsy; part of them have remained greatly behind in development. | A great number of the larvæ have died, without marked signs of abdominal dropsy. The survivors only show arrest of development. | A few larvæ have died without signs of abdominal dropsy. The survivors only show delayed development. | A few larvæ died without signs of abdominal dropsy. |
| All remaining larvæ were dead on the 24th day. | All larvæ died within 32 days after radiation, without a sign of abdominal dropsy. | All animals had died by the 27th day after radiation, without distinct signs of abdominal dropsy. | Only a few larvæ are alive on 28th day after radiation. They only showed arrest of development until their final demise. |

This table shows that the symptoms of radiation sickness appear especially distinctly if the larvæ are still contained within the membranes at the time of radiation.

The death of the irradiated larvæ from the same dose occurs the earlier the younger the larvæ are at the time of radiation. This early death may be convenient for the rapid disposition of the observation material. The earliest stages of development, however, possess the disadvantage that we cannot recognize whether barren, sterile eggs are not contained amongst the eggs. And further death by radiation often occurs so rapidly that one cannot always clearly decide whether the larvæ have perished on account of the radiation, because the symptoms of radiation disease have as yet not been distinctly formed.

We regard the state of development as the most favorable for purposes of investigation which lies between the morula stage and the time of escape of the larvæ from the egg.

### *Sensitiveness of the Frog Larvæ to the action of X-ray and Gamma-Rays.*

The second condition which we placed on the usefulness of a test object was that the biologic action should be clearly expressed in differently marked degrees with slight differences in dose. We termed it the biologic sensitiveness of the test object.

To obtain values free from any objection on this point we performed experiments with increasing doses during the stage of development, namely, between the gastrula stage and the stage in which the larvæ commence to assume the form of the tadpole within the membranes.

In the first of the experiments the dose was increased twofold. The spawn clump of a pair of rana esculenta served as observation material. The eggs were so far developed that the embryos within the membrane had already assumed shape and form. See Fig. 1, table II. This starting material was divided into three parts, each of thirty eggs. Parts I and II were placed in a bowl and each one radiated at the same time, each with a Coolidge tube. The distance of the focus to the spawn (FH) of both Coolidge tubes was chosen so that the dose measured with the ionization method applied to spawn I was twice as large as that applied to spawn II, therefore 200 and 100 e. The filter consisted of 1 mm. copper.

Part III was kept as a control in the same room in a glass bowl of the same dimensions as the others and upon the same glass frame. This spawn was protected from the rays during the time of the radiation.

After radiation the three groups were placed in three large culture bowls, the pond water was renewed daily and the spawn was reared in the manner already described.

*Extract from the observation journal.* Day of radiation: June 25th.

*Days of observation*:

June 28.—All the larvæ have left the membranes. In both series of radiated animals the characteristic symptoms of radiation sickness are seen. They are more distinctly marked in the animals rayed with the double dose. See figure 2, table II. The controls are developing normally.

June 30th.—The symptoms of radiation sickness have not progressed in comparison to the observation made June 28th. The controls have markedly advanced in growth in comparison to the radiated animals. See figure 3, table II.

July 2nd.—The animals radiated with the double dose have died, with the exception of two individuals. Nine animals radiated with the single dose are still living. The symptoms of radiation sickness are in most cases more marked in the animals radiated with the double dose than in those radiated with the single dose. The controls are all alive and of normal development. See figure 4, table II.

July 5th.—All radiated animals were dead on July 3rd. The controls are alive and of normal development.

After we had thus demonstrated that the sensitiveness of the test object is so great that plainly visible biologic differences in the reaction may be observed with the double dose we attempted in the following year at the spawning time of rana temporaria to determine still more exactly the sensitiveness.

*Course of the Experiment.*—The spawn clump of a pair of rana temporaria served as observation material. The eggs were so far developed that the embryos had developed to the gastrula stage within the membranes. The spawn clump was divided into five parts, each of about 100 eggs. One of them served as control, the other four were subjected to radiations.

The raying commenced four days postpartum, March 28th and was performed so that the four clumps were placed in four radiation stands and were exposed to the rays at the same time. A Coolidge tube, which was operated with an inductor and gas interrupter so that the potential energy in the tube corresponded to a parallel spark gap of 35 cm., served as radiation source.

The distance of the focus of the X-ray tube from the ionization chamber around which the four supports containing the animals were evenly placed, amounted to 35 cm.

The doses applied to each one of the four clumps of larvæ were 75, 100, 125 and 150 e. The individual successive doses therefore differ from each other by 25 e.

The filter was 10 mm. aluminum.

The result has been reproduced in the following table.

It follows from these investigations that the frog larvæ show a sensitiveness, if they are exposed to rays during a stage of development corresponding to that of the gastrula, that with a difference of dose of about 25 per cent a distinct difference in the biological reactions is just discernible, both as regards the mortality and the intensity of the symptoms of radiation sickness.

## SENSITIVENESS OF THE LARVÆ OF FROGS TO X-RAYS

Stage of development of the larvæ on the day of radiation: The larvæ are 4 days old. Four days postpartum (Partus March 24, at 12 A.M.). The larvæ are still within the membranes and evince about the stage of gastrula. Day of radiation: March 28. All animals have been rayed on the same day, at the same time and with the same tube. Filter: 10 mm. aluminum.

| Day of observation | Dose = 75 e | Dose = 100 e | Dose = 125 e | Dose = 150 e | Controls |
|---|---|---|---|---|---|
| 10 days after radiation | All the larvæ are still in the membranes and in comparison to the controls have developed very little, are about 4 mm. long, and a few show the characteristic deformities (curving). | All the larvæ are in the membranes, 4 mm. long, and most of them show the characteristic deformities. Half of the larvæ have died. | The larvæ show severe radiation sickness. They have grown to only 3 mm. in length, and show lumpy distensions. Most of the animals are dead. | Differences in these larvæ from those rayed with 125 e are not seen; the symptoms of disease are the same. However, the mortality is greater; only a few of the larvæ are still alive. | All the larvæ have left the membranes and swim about in the hatching bowl. They are 10 mm. long. |
| 12 days after radiation | The larvæ have escaped from the membranes, have developed somewhat, are 5 mm. long and just show the characteristic deformities. All the animals died on the 17th day of observation. | The larvæ have escaped from the membranes, are 5 mm. long and show slight indications of characteristic deformities. The animals died the evening before the day of observation. | All animals are dead. | All animals are dead. | The larvæ already show well-defined trunks and tails. |

*The Facility to procure Frog Larvæ of the same Origin in such large Numbers that the Results of Investigations cannot become marred by Individual Differences.*

The third factor which we placed on a biologic object is fulfilled by using the frog larvæ as test objects. The number of the procurable eggs is very large and it is possible to easily obtain eggs from one source in sufficiently large numbers as the female frog bears her spawn in a conglomeration of one clump. It is only necessary to determine by tests how large the individual differences in the eggs of one family are, to deduce therefrom the minimum of eggs necessary for each test. Our investigations showed, first, that the individual differences are much greater in older frog larvæ than in the young, as long as the latter are still contained within the membranes. This is perhaps dependent on the fact that the moment the

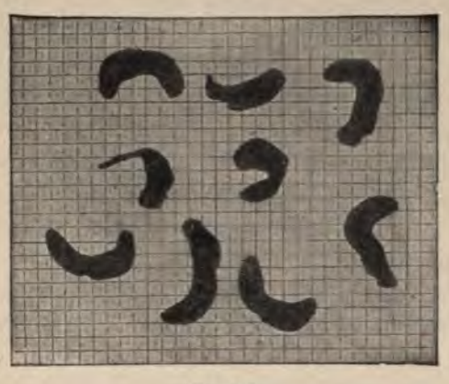


FIG. 46.

frog larvæ escape from the membranes, the various external conditions, above all nutrition, gain a determining influence on the development and capability of resistance of the larvæ.

This view gains justification by the fact that the control animals also after expulsion from the membranes soon show a not unessential difference in development.

On account of this reason the young frog larvæ are preferable to the older.

The differences in reaction are so slight in the young individuals that one may draw definite conclusions from a number of about fifty experimental animals in each test, as shown from our experiments. We reproduce in a photogram a number of larvæ which were taken at random from a group of fifty eggs radiated with the same dose under like conditions.

The photograph, Fig. 46, shows clearly that the difference in the intensity of the symptoms of radiation sickness is relatively small in

the composition of the rays filtered with 1 mm. copper. This has been demonstrated in our physical investigations. The gamma-rays of radium and mesothorium are perhaps still better defined in regard to their composition. Still we preferred the X-rays filtered with 1 mm. copper because it is difficult to measure the gamma-rays striking a more extensive biologic object on account of the impossibility to construct a radiation field of a somewhat homogeneous intensity when using radioactive substances.

For this reason we have compared the biologic action of the most varied kinds of rays, including also the gamma-rays, with the biologic action of X-rays filtered with 1 mm. copper.

Results from biologic experiments can only then be compared with each other, if in the details of the test the requirements have been observed which must be placed on unobjectionable comparative biologic tests. This request was fulfilled if frog spawn was used as a test object under the following prerequisites:

1. The frog eggs used for comparative experimental purposes must be derived from *one* family.

2. Results may only then be compared with each other if the experiments have been carried out at *the same time.*

3. The frog eggs must be of the same size and must be exposed to the rays in an equal thickness of layer.

4. The number of the eggs chosen for the test must not be too small on account of the great individual differences in the eggs of the same family.

5. During the experiment all other factors which could eventually exert a damaging influence on the frogs' eggs except X- and radium-rays must be avoided.

6. Following the experiments the radiated eggs must be kept under the same conditions of living.

As comparative investigations on the dependence of the intensity of the biologic action on the hardness of the rays in frogs larvae always require a very long time, because they demand repeated control tests, and as we may obtain the young frog larvæ only at a certain time of the year, we began with the investigations as soon as the physical investigations had so far progressed that a dosimeter could be placed at our disposal, which possessed the desired sensitiveness and dependence. If these conditions, sensitiveness and dependence, were fulfilled the results obtained could be used without any objections, even if later a correction had to be made in the event that the dosimeter did not meet the requirements demanded in the physical part. We used as dosimeter in these biologic tests the iontoquantimeter. The walls of the measuring chamber consisted of $\frac{1}{10}$ mm. aluminum. All results were obtained with the dosimeter which is described on page 59.

After the biologic experiments had been concluded the physical investigations revealed that a source of error existed attributable to

the use of aluminum in the construction of the walls of the measuring chamber. This error could be eliminated by the substitution of graphite for the aluminum in the walls of the chamber. The results obtained in the experiments on the dependence of the intensity of the biologic action on the hardness of rays must therefore be subjected to a definite correction. We did not attempt this correction in the recitation of these experiments to avoid unnecessary confusion. However the necessary correction in the summaries has been discussed in detail in a special chapter.

### Comparative Investigations on the Intensity of Biologic Action of X-rays Unfiltered and Filtered with 1 mm. Copper on Frog Larvæ

We observed that X- and gamma-rays by their action on frog larvæ produce characteristic changes in form and shape which finally may lead to the death of the individual. We have further seen that the early or late appearance of these symptoms is under otherwise like conditions dependent on the size of the applied dose. These accidents in the development of the frog larvæ due to the action of rays will be designated hereinafter as the biologic action of rays on the frog larvæ, and *by the different intensity of the biologic actions will be understood the difference in the degree of the injury as to time of occurrence as well as to the intensity of the symptoms.*

Course of the experiment: The spawn clump from a pair of rana esculenta served as observation material. The eggs had so far developed that the embroyos had just left the membranes.

This material was divided into three parts, each of fifty individuals. Parts 1 and 2 were brought in two different glass troughs filled with pond water and placed beneath the tube stand. Parts 1 and 2 were rayed at the same time each with a Coolidge tube. In the radiation of part 1 the X-rays were filtered with 1 mm. copper; in part 2 the X-rays were unfiltered. Part 3 was kept as control in a glass trough of the same dimension as those used for parts 1 and 2. The spawn was protected from the rays during the duration of the radiation in the X-ray room.

The distance of the focus of both Coolidge tubes from the surface of the frog spawn was chosen so that the intensity measured with the ionization method was as nearly alike as possible in the unfiltered X-rays and in those filtered with 1 mm. copper. The time duration of the radiation therefore was as uniform as possible.

80 e were applied in 83 and 89 minutes as the doses best suited for these experiments.

Subsequent to the radiation the three groups were placed in three large culture plates, the pond water was replaced daily. The algæ attached to the water plants and later steamed salad served as food for the frog larvæ.

*Extract from the observation journal.* Day of radiation: June 20th.

*Days of observation:*

June 24th—Distinctly visible changes are not seen in the radiated animals and controls.

June 26th—One animal of those radiated with X-rays filtered with 1 mm. copper has died; none of the animals radiated with unfiltered X-rays succumbed, but two of the controls. The radiated animals begin to show symptoms of radiation disease. However, they are not yet characteristic.

June 28th—Two of the animals rayed with X-rays filtered with 1 mm. copper have died; also three of the animals rayed with unfiltered rays and two of the controls. The greater number of the radiated animals in part 1 as well as part 2 now evidence distinct action of the rays, for they have markedly remained behind in growth in comparison with the controls.

June 30th—Of the animals rayed with X-rays filtered with 1 mm. copper none have died, five of the animals rayed with unfiltered rays and none of the controls. The radiated animals in comparison with the controls show well-pronounced retardation in growth. The animals rayed with unfiltered rays have perhaps remained somewhat more behind in growth than those radiated with X-rays filtered with 1 mm. copper.

July 2nd—Another one of the animals rayed with X-rays filtered with 1 mm. copper has died, an additional five of those rayed with unfiltered X-rays have succumbed, but none of the control animals. Otherwise the findings are the same as on June 30th.

July 5th—Seven of the animals rayed with X-rays filtered with 1 mm. copper have died and twelve of those rayed with unfiltered X-rays, but none of the controls.

Between groups 1 and 2 a difference may be observed in so far as the animals rayed with X-rays filtered with 1 mm. copper have several marked vesicular distentions in the abdominal region; they cannot be observed in the animals radiated with unfiltered X-rays.

Six of the animals radiated with X-rays filtered with 1 mm. copper, that is, all those showing abdominal dropsy on July 5th have died; three of those radiated with unfiltered X-rays, and none of the controls. The surviving animals do not show any special characteristic symptoms of radiation disease. However they have assumed a more ball-like shape in comparison to the controls which show a somewhat lengthy form. The radiated animals are also less strongly pigmented and much more transparent than the controls. The animals radiated with unfiltered X-rays have perhaps remained somewhat more behind in growth than the animals radiated with X-rays filtered with 1 mm. copper.

July 10th: Thirteen of the animals radiated with X-rays filtered with 1 mm. copper are still alive and five of those radiated with unfiltered X-rays. None of the controls have died.

*Control Experiment.*

*Course of Experiment.*—The spawn clump of a pair of rana esculenta served as radiation material. The eggs had so far developed that the embryos had just left the membranes and were swimming about on the culture plate.

The details of the experiment were the same as in the first experiment. The dose was 80 e.

*Extract from the observation journal.* Day of radiation, June 8th.

*Days of observation:*

June 14th—The controls are all alive and of normal development. The animals radiated with X-rays filtered with 1 mm. copper and those radiated with unfiltered rays show distinct retardation in growth in comparison with the controls. A recognizable difference does not exist between the radiated groups.

June 16th—One of the animals radiated with X-rays filtered with 1 mm. copper has died showing dropsical swellings. Several of the individuals radiated with unfiltered rays evidence dropsical swellings. None of the animals of this group have succumbed. Both radiated groups have markedly remained behind in growth in comparison to the controls.

June 18th—A large number of animals radiated with X-rays filtered with 1 mm. copper have died; also a few of the animals radiated with unfiltered rays.

The animals radiated with X-rays filtered with 1 mm. copper show a somewhat more marked arrest in development than the animals radiated with unfiltered rays.

June 22nd—All except nine of the animals radiated with X-rays filtered with 1 mm. copper are dead. The greater number of animals radiated with unfiltered rays are alive and perhaps show a somewhat slower growth than the animals radiated with X-rays filtered with 1 mm. copper.

June 24th—Same findings as on June 22nd.

June 26th—Same findings as on June 22nd. The observations were continued to the end of July, without any essential change being apparent in the observations.

*From the two experiments it follows, that with the same dose and with the same intensity, measured with the aluminum chamber, the unfiltered X-rays do not exert a more markedly pronounced stronger action on frog spawn than the X-rays filtered with 1 mm. copper.*

## Comparative Investigations on the Intensity of the Biologic Action of X-rays Filtered with 3 mm. Aluminum and 1 mm. Copper

*Course of the Experiment.*—The spawn clump of a pair of rana esculenta served as observation material. The eggs had so far developed that the embryos had just assumed form within the membranes. (See Fig. 1, table III.)

This starting material was divided in three parts: Parts 1 and 2 were each placed in glass troughs filled with pond water. These were arranged underneath the tube stand and radiated at the same time with a Coolidge tube. To part 1 X-rays filtered with 3 mm. aluminum and to part 2 X-rays filtered with 1 mm. copper were applied. Part 3 was kept in a similar glass trough and protected from the rays during the duration of the radiation. The distance of the foci of both Coolidge tubes from the surface of the frog spawn was chosen so that the intensity of both radiations, i.e., the time durations of radiation were as nearly alike as possible. The duration of the radiations was 71, respectively 64 minutes.

After radiation the groups of spawn were reared in the usual manner.

*Extract from the observation journal.* Day of radiation: June 8th.

*Days of observation:*

June 14th—All the embryos, radiated and non-radiated, have left the membranes. All the controls are alive. Most of the animals radiated with X-rays filtered with 3 mm. aluminum and with 1 mm. copper already evince the characteristic dropsical swellings and the curious retardations in development of the body. A difference is observable in the radiated groups in so far as the radiation symptoms in the animals radiated with X-rays filtered with 1 mm. copper are somewhat more pronounced, also a larger per cent of these groups has died. (Figs. 2, 3, 4, table III.)

June 16th—All controls are alive and of normal development. The animals radiated with X-rays filtered with 1 mm. copper show the characteristic disturbances of development much more pronounced than the animals radiated with X-rays filtered with 3 mm. copper.

June 18th—All of the controls are alive and show normal development. An additional number of animals radiated with X-rays filtered with 1 mm. copper has succumbed with severe symptoms of radiation sickness. Only one individual of the animals radiated with X-rays filtered with 3 mm. aluminum has died. In this group the retardations of development in the survivors are less marked than in those radiated with X-rays filtered with 1 mm. copper.

June 22nd—All the controls are alive and of normal development. All the animals, except four, radiated with X-rays filtered with 1 mm. copper have died. The four survivors show the characteristic radiation symptoms. Of group 2 no other animals have perished. The characteristic disturbances of development have not essentially progressed. (Figs. 5, 6, 7, table III.) In the photographs also the greater transparency and the more ball-like form of the radiated larvæ is plainly recognizable.

June 24th—The controls are all alive and of normal development. All except one of the animals radiated with X-rays filtered with 1 mm. copper are dead. The animals radiated with X-rays filtered with 3 mm. aluminum do not evidence an essential progress in the arrest of development. (Figs. 8, 9, 10, table III.)

June 26th—The controls are all alive and of normal development. An additional animal of group 2 has succumbed. The survivors do not show a progressive disturbance of development in comparison to the findings of June 22nd.

The observation was continued until August 1st. Characteristic swellings and deformities were not seen in the surviving animals radiated with X-rays filtered with 3 mm. aluminum. The only influence of the radiation is recognized in the marked arrest of growth and the greater mortality in contradistinction to the controls.

*Control Experiment.*

*Course of Experiment.*—As observation material served the spawn clump of a pair of rana esculenta, in which the eggs had progressed for far in development that the embryos already showed movements within the membranes.

The dose applied was 80 e. The details of the experiment were exactly the same as those of the preceding experimnt.

*Extract from the observation journal.* Day of radiation: June 9th.

*Days of observation:*

June 14th—All of the embryos, radiated and non-radiated, have left the membranes. The control animals are alive. All the radiated animals show plainly discernible vesicular swellings and arrest of development. However, a difference exists in so far as a greater percentage of the animals radiated with X-rays filtered with 1 mm. copper have died.

June 16th—All the controls are alive and show normal development. The animals

radiated with X-rays filtered with 1 mm. copper show the characteristic disturbances of development more plainly than those radiated with X-rays filtered with 3 mm. aluminum.

June 18th—All the controls are living and of normal development. All the animals radiated with X-rays filtered with 1 mm. copper are dead, while of group 2 only a part has succumbed. The surviving animals show pronounced arrest of growth in comparison to the controls.

June 22nd—All the controls are living and of normal development. All of the animals of group 2, except three, are dead. The survivors do not evince any other radiation symptoms except arrest of growth.

In the following year the experiments were repeated with the same details with rana temporaria as well as with rana esculenta. These tests also revealed the same results.

*We conclude from the experiments that with like dose and with like intensity, measured with the aluminum chamber, the X-rays filtered with 3 mm. aluminum have a weaker biologic action on frog spawn than X-rays filtered with 1 mm. copper.*

## Comparative Investigations on the Intensity of the Biologic Action of Gamma-Rays of Radium and Mesothorium Filtered with 1.5 mm. Brass Plus 5 mm. Celluloid and X-rays Filtered with 1 mm. Copper

We repeat the following experiments from numerous similar investigations.

*Course of the Experiment.*—The spawn clump of a pair of rana esculenta served as observation material. The eggs were so far developed that the embryos just assumed form within the oval membranes. (Fig. 1, table IV.)

From this starting material fifty eggs were radiated with X-rays and fifty with gamma-rays according to the details enumerated in the preceding experiments.

Part 1 was radiated with the radium cannon, which was mounted as previously described. The distance of the celluloid from the frog spawn was 2 cm. Part 2 was radiated with a Coolidge tube, which was placed at such a focus distance from the frog spawn that the same intensity would be secured and the time duration of the application would be the same in both series. Both radiations lasted thirteen hours. The dose was 80 e. After the radiation the radiated frog eggs were reared in the usual manner.

*Extract from the observation journal.* Day of radiation: May 31st.

*Days of observation:*

June 4th—The radiated and non-radiated embryos have left the membranes. The controls are all alive and show normal development. (Fig. 2, table IV.) The animals radiated with gamma-rays evidence the characteristic symptoms of radiation sickness. (Fig. 3, table IV.) The animals radiated with 1 mm. copper evidence only slight changes, the blister formation is absent; in comparison to the controls a slight deformity of the larvæ is noticeable in both radiated groups. (Fig. 4, table IV.)

June 5th—All the animals radiated with gamma-rays have died. The controls and the animals radiated with X-rays filtered with 1 mm. copper are alive.

Of the animals radiated with X-rays a few show spasm-like motions, otherwise no marked differences exist between these and the controls. (Fig. 3, table V.)

The animals were kept under observation until the end of June. In the meantime the front and hind legs had developed. The radiated animals show a much more pronounced pigmentation in comparison to the non-radiated animals. (Fig. 4, table V.)

*It is shown that with like dose measured with the aluminum chamber the gamma-rays of radium and mesothorium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid applied to larvæ of rana temporaria of an advanced development, have a stronger biologic action than the X-rays filtered with* 1 *mm. copper.*

## Numerical Determination of the Dependence of the Intensity of the Biologic Action on the Hardness of the Rays; the Biologic Factor

The experiments just recorded demonstrated that the biologic action of the various hardnesses of rays for the same dose measured with aluminum chambers is of varying intensity. It must be our endeavor to express this difference in the intensity of the action of the various kinds of radiations if possible numerically, i.e., to find the biologic factor of the difference in intensity of action of the various kinds of rays.

The biologic factor means the numerical which indicates how much stronger one kind of ray acts biologically than another variety of ray with like dose. For the determination of this factor we will adopt as standard of comparison the X-rays filtered with 1 mm. copper on account of their excellent constancy. The frog larvæ are well suited as test objects for this numerical determination, because their sensitiveness is relatively great.

We do not need to determine the biologic factor between rays unfiltered and filtered with 1 mm. copper because appreciable differences in the intensity of the biologic action on frog larvæ between these two varieties of rays hardly exist.

A difference just recognizable in the biologic action between X-rays filtered with 3 mm. aluminum and 1 mm. copper was observed. We will attempt to determine the biologic factor for these radiations.

## Determination of the Biologic Factor Between X-rays Filtered with 3 mm. Aluminum and with 1 mm. Copper

We know from the experiments on the sensitiveness that the test object already reacts with a difference just recognizable in the intensity of the biologic action if a difference in the dose of 25 per cent exists. The biologic factor between X-rays filtered with 3 mm. aluminum and 1 mm. copper must be about 0.75.

same experiments were again undertaken, observing the same details of method. The results were analogous to those reported above.

*We conclude from all the experiments that with the same dose, measured with the aluminum chamber, the gamma-rays of mesothorium and radium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid possess a very much stronger biologic action on the larvæ of frogs than X-rays filtered with* 1 *mm. copper.*

It being the first time that such an explicitly stronger biologic action of the gamma-rays of radium and mesothorium in contradistinction to X-rays filtered with 1 mm. copper, with like dose, measured with the aluminum chamber, had been recognized, we thought it important to determine whether such differences would also appear in frog larvæ less sensitive on account of a more advanced stage of development. For this reason older larvæ were employed as radiation material in the following experiment. The larvæ had escaped the membranes three days previously.

From this material fifty larvæ were radiated with X-rays and fifty with gamma-rays in the manner above described, while fifty larvæ served as controls.

The time duration of radiation for the larvæ rayed with X-rays filtered with 1 mm. copper was three hours. In contradistinction to the preceding experiment in which we used the same dose and the same intensity we chose in this experiment the same dose but not the same intensity.

To render the influence of the age of the frog larvæ as negligible as possible on account of the long time duration of the radiation with the radium cannon in contrast to the relatively short duration of radiation with X-rays, the three hour radiation with the roengen tube was exactly placed in the middle of the time duration of radiation of thirteen and one-half hours with the radium cannon. The dose was about 83 e.

*Extract from the observation journal.* Day of radiation: April 19th to 20th.

*Days of observation:*

May 4th: The controls are all alive and show normal development.

The animals radiated with gamma-rays have remained considerably behind in growth in contrast to the animals radiated with X-rays. The latter, however, show arrest of growth in comparison to the controls, though not so marked as in the other group of radiated animals. (Fig. 1, table V.) The latter show a decreased appetite for food and execute peculiar spasmlike movements when touching the glass bowl. Both groups of radiated animals are less sensitive to blows against the glass walls than the controls.

May 14th: The controls are all alive and of normal development.

The animals radiated with gamma-rays evidence still more pronounced retardations of growth and characteristic spasmlike movements. They are beginning to die. The animals radiated with X-rays have remained somewhat behind in growth in comparison to the controls, but it seems as if the differences in size tend to become equalized. (Fig. 2, table V.)

May 18th: Of the animals radiated with gamma-rays, all except two have died. These evince quite marked arrest of growth in comparison to the controls.

temporaria, and in June at the spawning time of rana esculenta, the same experiments were repeated with the same details as a control. These also revealed without exception the same results.

## Determination of the Biologic Factor Between Gamma-rays of Radium and Mesothorium Filtered with 1.5 mm. Brass Plus 5 mm. Celluloid and X-rays Filtered with 1 mm. Copper

The preceding experiments had already demonstrated that the biologic action of gamma-rays was considerably stronger than that of X-rays filtered with 1 mm. copper. Therefore we proceeded in the determination of the biologic factor so that the dose of gamma-rays of mesothorium and radium, filtered with 1.5 mm. brass plus 5 mm. celluloid was 80 e, and that of the X-rays filtered with 1 mm. copper was progressively 80 e, 160 e and 240 e.

If we had maintained the same intensity of the rays in these experiments as in the preceding ones, the differences in the time durations to obtain the doses mentioned for the various groups would have become quite great. Since the intensity of the symptoms is strongly influenced by the stage of development of the larvæ, we had to dispense with the same intensity in these experiments. We chose the time duration of radiation with the X-rays so that it concurred as closely as possible with the radiation of radium and mesothorium. The influence of the difference in intensity is of such slight importance on the intensity of the biologic action, that it may be disregarded. This point will be proven in a later chapter. The duration of radiation with radium and mesothorium to apply a dose of 80 e amounts to thirteen hours. Within this time the various doses of X-rays could be applied.

*Course of the experiment:* Day of radiation June 20th.

*Days of observation:*

June 24th: The larvæ have left the membranes.

The majority of the animals radiated with gamma-rays evidence the characteristic symptoms of the radiation disease.

The findings in the animals rayed with X-rays are as follows:

Only a few of the animals radiated at the beginning of the radiations with 80 e show insignificant vesicular swellings, the others did not remain behind in development in comparison to the controls.

Almost all the animals radiated with a dose of 160 e show distinct retardation in growth in comparison to the controls; on the other hand, no symptoms of radiation disease worth mentioning are present.

The animals radiated with 240 e show distinctly the characteristic symptoms of the radiation disease as dropsy and deformities in about the same degree as the animals radiated with gamma-rays.

An additional group of animals serving also as controls and radiated with 80 e at the termination of the radiation show the same findings as the animals radiated with 80 e at the beginning of the radiation.

Of the fifty animals radiated with gamma-rays, twenty-four died with the characteristic symptoms of the radiation disease.

The animals radiated with X-rays show the following casualties:

Of the animals radiated with 240 e, fifteen succumbed with the characteristic symptoms of the radiation disease.

Of the animals radiated with 160 e, eight died. These and the surviving animals show the characteristic symptoms of the radiation disease. However, they did not remain behind in growth to the same degree as the animals radiated with gamma-rays and with 240 e X-rays.

The animals radiated with 80 e at the beginning and termination of the radiation do not show any differences among themselves. Both groups evince slight retardations in growth, but hardly any symptoms of the radiation disease. Of the animals radiated with 80 e at the beginning of the experiment, three are dead; of those radiated at the conclusion of the experiment, four are dead.

July 2nd: All the animals radiated with gamma-rays are dead.

The findings in the groups radiated with X-rays are as follows:

Those radiated with 80 e at the beginning of the experiment are all dead. Of those radiated with 80 e at the end of the experiment, one died. The survivors show marked arrest of growth in comparison to the controls.

The animals radiated with 160 e and 240 e have all died except one. They have perceptibly remained behind in growth in comparison to the controls.

July 5th: The surviving animal radiated with 160 e is dead.

Of the animals radiated with 80 e at the end of the radiation, six have died. The survivors evince still more distinctly the retardation in growth in comparison to the controls.

July 7th: Of the animals radiated with 80 e at the end of the radiation, an additional seven have died. The controls are all alive. The findings are otherwise the same as on July 5th.

July 10th: The survivors of the animals radiated with 80 e are alive, but show pronounced retardation in growth in comparison to the controls, which are all living.

*From this and two additional experiments with the same results it follows, that the biologic factor, determined with the aluminum chamber, between gamma-rays of radium and mesothorium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid and X-rays filtered with* 1 *mm. copper is at least* 3.

To determine the biologic factor still more exactly, additional experiments were arranged so that the quadruple dose of X-rays in comparison with the single dose of gamma-rays was applied.

The time duration of the radiation with radium and mesothorium was thirteen hours, that of the X-rays amounted to the same time. The details of the experiment were otherwise the same as in the preceding ones. The doses applied were 80 e and 4 x 80 e.

*Extract from the observation journal.* Day of radiation: July 3rd.

The embryos have just assumed form within the membranes and execute voluntary movements. (Fig. 1, table VII.)

*Days of observation*:

July 5th: The larvæ have all left the membranes. The controls are alive and of normal development.

Of the animals radiated with 320 e X-rays, one has died; of those radiated with 80 e gamma-rays, also one. The animals of these groups have remained behind in growth in comparison to the controls; they already evidence the first symptoms of the radiation disease. A difference in the degree of the disease symptoms cannot be determined. (Fig. 2, table VII.)

July 7th: The controls are all alive and of normal development.

None of the animals radiated with 320 e X-rays succumbed. All of the animals radiated evince characteristic disease symptoms. The animals radiated with 320 e X-rays

have remained less behind in growth than those radiated with 80 e gamma-rays. (Fig. 3, table VII.)

July 8th: The symptoms of the radiation disease are very strongly pronounced in the radiated animals of both groups.

July 9th: All the animals radiated with gamma-rays are dead; twenty-eight of those radiated with X-rays are still alive.

July 10th: All of the animals radiated with X-rays except three succumbed. The controls are all alive and have continued to develop normally. (Fig. 4, table VII.)

*The biologic factor, determined with the aluminum chamber, between gamma-rays of radium and mesothorium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid and the X-rays filtered with* 1 *mm. copper must be placed between* 3 *and* 4 *based on these experiments.*

The same experiments with the same details were repeated as controls during March of the following year; they also revealed, without exception, the same results.

# Investigations Concerning the Dependence of the Intensity of the Biologic Action on the Hardness of the Rays in Human Tissues

We had convinced ourselves by experimental tests in animal organisms of a low order—the frog spawn of rana esculenta and rana temporaria—that definite laws for the biologic action of the various hardnesses or qualities of rays can be formed. We then investigated whether these laws on the biologic influence of the various hardnesses of rays may be applied to *human tissue.*

We had an opportunity to instigate observations on three kinds of tissues:

a. The human skin,
b. Carcinomata,
c. The human ovary.

In all therapeutic applications to deep-seated carcinomata we are of necessity compelled to apply to the skin above them such a dose that symptoms of irritation in the skin ensues.

These irritations are expressed in characteristic changes, the so-called erythema formation, which appear in varying intensities from the simple browning of the skin to reddish discoloration and erythema. We may use these variously intense irritation symptoms of the skin as tests, similar as in the frog spawn, to form an opinion of the various biologic actions of the different hard rays investigated in the previous chapter.

We naturally could use only such observations of therapeutic radiations in which all the requirements were fulfilled which we must place upon comparative biologic observations. These are as follows:

1. The observations must be made on *one and the same* person if possible.

2. The radiations with the various hard rays must be applied *at the same time.*

3. The radiated skin surfaces must be of the *same size* and must not pass below a certain minimum size.

4. The radiated skin surfaces must be confined to *homogeneous regions* of the body. Comparative observations on the action of various kinds of rays on the skin, for instance abdomen and back, can only be used with reservations on account of the different behavior to rays of these topically different regions of the skin.

## Observations on the Sensitiveness of the Human Skin to the Action of Filtered X-rays

It is only then possible to confirm the laws in reference to the skin if it is apparent that the skin is sufficiently sensitive, that is, that it reacts differently to a sufficiently small difference of dose.

In order to apply to a deep-seated cancer a lethal dose, it is necessary to subject the skin to the limit of tolerance, especially in individuals suffering from gastric cancer which is influenced with difficulty. The radiation was carried out so that we might obtain an idea of the sensitiveness of the skin of these patients by applying various sized doses to the different fields of skin. It is often required in order to influence cancer to ray the skin so intensively that it answers with an erythema.

The fields thus radiated may then also serve for the observation on the determination of the sensitiveness of the skin.

In a patient suffering from an inoperable cancer of the stomach two fields of a size of 6 by 8 cm. were symmetrically placed above the umbilicus and surrounded by heavy lead sheets. The space between the fields was 2 cm. The fields were rayed on the same day with the same Coolidge tube, a focus skin distance of 50 cm. and a filter of 10 mm. aluminum. The measuring chamber of the iontoquantimeter was placed so that about one-half of it was pressed into the skin.

The dose of the field *a* amounted to 145 e; of field *b*, to 185 e.

| *Field a* | *Field b* |
|---|---|
| *Day of radiation*, Oct. 9, 1916. | *Day of radiation*, Oct. 9, 1916. |
| *Days of observation:* | *Days of observation:* |
| Nov. 14, 1916. A very light reddening is seen. (Fig. 1, table VII.) | Nov. 14, 1916. A plainly visible red discoloration and formation of minutest vesicles is seen over the entire field. |
| Dec. 9, 1916. Erythema gone. | Dec. 9, 1916. Light brownish discoloration of skin. |

*From these and similar observations we may state that the human skin possesses a sensitiveness to filtered X-rays which shows a marked difference in the intensity of the biologic action with a difference in the size of dose of about* 25 *per cent.*

Since the sensitiveness of the human skin is the same as the sensitiveness of the frog spawn in its early state, the same laws seen in the frog larvæ may be observed in the human skin, if analogous areas of the skin are used.

## Comparative Observations on the Intensity of the Biologic Action of X-Rays Filtered with 3 mm. Aluminum and 1 mm. Copper on the Skin

To determine the difference in the degree of the biologic action on the skin of X-rays filtered with 1 mm. copper and X-rays filtered

with 1 mm. aluminum we performed many observations. We will repeat only a few of the observations characterized by differently intense erythemata.

*Observation* 1. Case S. Two fields of a patient with inoperable intestinal cancer were radiated. Each field was of the size of 6 by 8 cm. The skin surrounding the fields was protected with lead plates of a thickness of 3 mm. Field 1 was located in the center in the median line 2 cm. beneath the umbilicus. Field 2 also was located in the center two fingers width above the umbilicus. The fields were radiated on two succeeding days with the same Coolidge tube and the same inductor with gas interrupter.

The aluminum chamber of the dosimeter was so pressed into the skin that the middle was even with the skin surface. The dose applied to each field was 167 e. The X-rays applied to field 1 were filtered with 1 mm. copper, those to field 2 with 3 mm. aluminum. The focus skin distance was selected so that the time duration of the application of the dose was about the same.

*Extract from the observation journal.*

Field 1. Radiated with 1 mm. copper.
*Day of radiation:* July 23, '15, from 4:10 P.M. to 7 P.M.
*Days of observation:*
Sept. 6, '15. An erythema of the skin of the field is just visible.
Sept. 15, '15. Erythema distinctly marked in form of a pronounced reddening of skin. (Fig. 1, table IX.)
Sept. 20, '15. Erythema somewhat paler than on Sept. 15. No formation of blisters.
Sept. 27, '15. Erythema now brownish red, without vesicles. (Fig. 3, table IX.)

Field 2. Radiated with 3 mm. aluminum.
*Day of radiation:* July 24, '15, from 10:20 A.M. to 12 noon.
*Days of observation:*
Sept. 6, '15. An erythema is nowhere to be seen.
Sept. 15, '15. A slight erythema in form of spots just beginning to appear. (Fig. 2, table IX.)
Sept. 20, '15. Erythema slightly stronger than on Sept. 15.
Sept. 27, '15. Erythema already fading. (Fig. 4, table IX.)

From this observation we see that with the same dose and the same intensity the X-rays filtered with 1 mm. copper have a somewhat stronger biologic action on the skin than the X-rays filtered with 3 mm. aluminum.

*Observation* 2. Case D. The course of the observation adhered closely to the one in Case 1. The dose, also, applied with the same instrument, was the same.

*Extract from the observation journal.*

Field 1. Radiation with 1 mm. copper, 165 e.
*Day of radiation:* Sept. 20, '15.
*Days of observation:*
Oct. 23, '15. A light reddening begins to appear.
Oct. 30, '15. Distinctly confluent reddening.

Field 2. Radiation with 3 mm. aluminum, 165 e.
*Day of radiation:* Sept. 20, '15.
*Days of observation:*
Oct. 23, '15. A light follicular reddening begins to appear.
Oct. 30, '15. Slightest follicular reddening.

Nov. 5, '15. Uniform and light erythema. (Fig. 1, table X.)
Nov. 13, '15. No change in findings of Nov. 5.
Nov. 17, '15. The reddening, which is very light, turns brownish. (Fig. 3, table X.)
Nov. 26, '15. Erythema has disappeared. Skin is almost normal.

Nov. 5, '15. General follicular and distinctly confluent reddening. (Fig. 2, table X.)
Nov. 13, '15. A slight confluent erythema of first degree, perhaps somewhat more intense than in Field 1.
Nov. 17, '15. Very light erythema, hardly of a first degree, fading to brown. (Fig. 4, table X.)
Nov. 26, '15. Erythema is gone, skin is almost normal.

*The result of this observation is that with the same dose and the same intensity the X-rays filtered with 1 mm. copper have almost the same biologic action on the skin as those filtered with 3 mm. aluminum.*

*Observation* 3. The course of the observation was kept closely adherent to the preceding ones. The dose was a higher one being 240 e.

*Extract from the observation journal.*

Case S.

Field 1. Radiation with X-rays filtered with 1 mm. copper.
*Day of radiation:* Sept. 11, '15.
*Days of observation:*
Oct. 16, '15. Beginning distinct browning of the radiation field.
Oct. 20, '15. The brown changes somewhat to red.
Oct. 25, '15. The erythema turns a bluish red tint. (Fig. 1, table XI.)
Oct. 30, '15. The erythema commences to fade, the skin turns brown. No formation of blisters.
Nov. 6, '15. Further fading of the browning. No loss of epithelium.
Nov. 13, '15. Very slight scaling of the skin.
Nov. 17, '15. The lamellæ have been shedded, a new normal skin appears which still looks delicate. (Fig. 3, table XI.)
Nov. 28, '15. The radiated skin is still lightly tanned. No formation of scars. Erythema has disappeared.

Field 2. Radiation with X-rays filtered with 3 mm. aluminum.
*Day of radiation:* Sept. 16, '15.
*Days of observation:*
Oct. 16, '15. Beginning distinct erythema of a more reddish tint than in Field 1.
Oct. 20, '15. The reddening has somewhat increased.
Oct. 25, '15. The erythema assumes a bluish red tint. (Fig. 2, table XI.)
Oct. 30, '15. The reddish discoloration has remained somewhat longer than in Field 1.
Nov. 6, '15. Marked desquamation of skin without formation of blisters.
Nov. 13, '15. After completion of desquamation, a new, somewhat delicate, skin appears.
Nov. 17, '15. Same findings as on Nov. 13. (Fig. 4, table XI.)
Nov. 28, '15. No formation of scars. Slight tanning of skin; erythema has disappeared.

*It follows from this observation that the result is the same as in the previous observation.*

From the three observations we conclude:

*With like dose and like intensity, measured with the aluminum chamber, the X-rays filtered with 3 mm. aluminum have a somewhat weaker biologic action on the skin than X-rays filtered with 1 mm. copper. This result, therefore, corresponds absolutely to the observations made in animal organisms.*

These observations together with the observations on the sensitiveness of the skin enables us to determine the biologic factor. We

saw from the observation on the sensitiveness that with an increase of the dose of 25 per cent distinct differences in the symptoms of irritation of the skin already appeared. In these last experiments the signs are just noticeable. Consequently the biologic factor is not smaller than 0.75.

### Comparative Observations on the Intensity of the Biologic Action on Gamma-Rays of Radium and Mesothorium, Filter with 1.5 mm. Brass Plus 5 mm. Celluloid, and X-Rays Filtered with 1 mm. Copper on the Skin

It is quite natural that in the cases therapeutically treated we have not any in which we could make observations in one and the same patient at the same time about the difference in the intensity of the biologic action of gamma-rays and X-rays filtered with 1 mm. copper. For a combined radiation upon the abdominal skin with gamma and X-rays we could not execute on account of uncontrollable and contrary facts. For instance, if we should choose two fields on the abdominal skin and radiate one field with gamma-rays and the other with X-rays, it would be impossible to protect the other field from the gamma-rays. The field reserved for the X-radiation would also receive a dose of gamma-rays as it would be impossible to sufficiently protect this field from the very penetrating gamma-rays. However, the field reserved for the gamma radiation may be effectually protected from the X-rays.

The first demand which we placed on comparative observations, namely that they must be carried on at the same time in one and the same individual, can therefore not be fulfilled. As we had at disposal a *great number* of observations in which an erythema could just be obtained with a definite dose of gamma radiations as well as of X-rays, we are enabled, from the comparison of the doses necessary for these results, to draw conclusions about the intensity of the biologic action upon the skin. The individual error becomes so strongly minimized by the large series of such observations, that it may be neglected, the more so as it became certain with the various kinds of hardnesses of rays used that the erythema dose in different individuals does not essentially vary. We must leave out of consideration a few cases which lie without the limits of these observations on account of their increased roentgen sensitiveness.

Of the cases treated with X-rays filtered with 1 mm. copper an erythema rarely appeared with a single dose below 165 e; with a dose of 165 e a light erythema, characterized by a slight, rapidly disappearing reddening with subsequent tanning, appeared in about 30 per cent; with a dose of 185 e a light erythema appeared in most of the cases; with a dose of 210 e an erythema of the second degree with desquamation of the skin, and in many cases formation of vesicles occurred in all the cases.

When radiating with gamma-rays of radium and mesothorium by means of the radium cannon above described, which was always prepared in the same manner with our preparations, experience obtained from our therapeutic radiations has taught us that a light erythema appeared in 60 per cent of the cases with an application lasting ten hours, and in 80 per cent of cases with an application lasting twelve hours. The dose, thus applied to the skin, was 58 e respectively 70 e.

If we arrange the doses opposite each other with which about the same irritation of the skin appeared when radiating with gamma-rays or with X-rays filtered with 1 mm. copper, it appears that the biologic action of the gamma-rays surpasses that of the X-rays filtered with 1 mm. copper. The ratio of the doses necessary for the production of the skin irritations give us at the same time the numerical size of the biologic factor. 60 e of the dose of the gamma-rays correspond to about 180 e of X-rays filtered with 1 mm. copper and both result in the same biologic action of the skin. We conclude:

*With same dose, measured with the aluminum chamber, the gamma-rays of radium and mesothorium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid, have an essentially stronger biologic action on the skin than X-rays filtered with* 1 *mm. copper. The biologic factor amounts almost to* 3.

Having thus seen that the laws on the intensity of the biologic action of the various hard rays on the human skin may be established analogously to those on the frog, we attempted to prove whether these laws also may be applied to superficially located carcinomata.

## Comparative Observations on the Intensity of the Biologic Action of X-rays Filtered with 3 mm. Aluminum and 1 mm. Copper on Surface Carcinomata

The requirements which we must place on comparative biologic observations to render them free of any objections, can be unfortunately fulfilled only to a small degree in these observations. In spite of this we endeavored to render the sources of error as small as possible by (1) making the observations on two carcinomatous nodules in one and the same person; (2) by applying the radiation with rays of different hardnesses and at the same time; and (3) by choosing carcinoma nodules and surrounding skin surfaces of as even a size as possible.

*Course of the Observation.*—The observation was made in a patient who suffered from an inoperable cancer of the right breast, which had caused numerous metastases in the glands and subepithelial metastatic skin nodules on the sternum of the left breast. Two of these metastic knots of the size of a walnut that had formed on and beneath the skin of the left breast were selected for radiation. Figs. 1 and 2, table XII, show these nodes in natural size. One of these

nodes *a* lying nearest to the sternum was radiated with X-rays filtered with 1 mm. copper, the other node *b* was radiated with X-rays filtered with 3 mm. aluminum. The aluminum chamber of the dosimeter was pressed down into the skin so that the middle longitudinal plane was even with the plane of the skin. The dose applied to each field was 165 e.

*Extract from the observation journal.*

The node *a* (Fig. 1, table XII) was radiated within a field the size of 7 x 7 cm.
*Beginning of radiation:* July 22, 1915, at 10:25 A.M. Termination at 12:50 P.M.
*Day of observation:* Sept. 15, 1921. The node *a* has disappeared to the senses of sight and touch. (Fig. 3, table XII.)
The node *b* (Fig. 2, table XII) was radiated within a field the size of 7 x 7 cm.
*Beginning of radiation:* July 22, 1915, at 3:50 P.M. Termination at 5:10 P.M.
*Day of observation:* Sept. 15, 1915. The node *b* has disappeared to the sense of sight. On palpation an infiltration the size of a hazelnut is felt. (Fig. 4, table XII.)

From this observation it follows that with like dose and like intensity, measured with the aluminum chamber, the X-rays filtered with 1 mm. copper have the same intensity of biologic action as X-rays filtered with 3 mm. aluminum as evidenced by a resorption of the cancer nodes which were located superficially.

We do not possess any additional observations, for the reason that X-rays filtered with 3 mm. aluminum are not well adapted for a uniformly penetrating radiation of cancer nodes on account of their relative softness.

## Comparative Observations on the Intensity of the Biologic Action of Gamma-rays of Radium and Mesothorium Filtered with 1.5 mm. Brass Plus 5 mm. Celluloid and X-rays Filtered with 1 mm. Copper on Carcinomatous Nodules of the Breast

We have only one case of bilateral carcinoma of the breast that can be applied to this observation.

Case E. *Extract from the history:*

*Left breast:* Mammilla inverted, firmly adherent to a flat tumor of a diameter of 5 cm., which is fixed to the pectoralis muscle. The axillary space is filled with about ten palpable glands the size of a cherry. Deeper located glands are not palpable; supraclavicular space is free.

*Right breast:* Hanging down, contains a movable tumor the size of two plums in the right upper quadrant, axillary and supraclavicular spaces are free.

An excision of tissue for microscopic examination from both breasts was made. Report from the pathologic institute Freiburg reads carcinoma.

*Day of radiation:* Sept. 28, 1915.
*Left breast:* The breast was rayed with the radium cannon, arranged in the manner

*Day of radiation:* Sept. 30, 1915.
*Right breast:* Radiation with X-rays filtered with 1 mm. copper, focus skin dis-

previously described. The radiation lasted thirteen hours; the dose applied was 76 e.

Dec. 8, 1915. Mammilla retracted. A freely movable tumor, the size of a nursing infant's fist, is palpable. Supraclavicular space is free. Six nodes about the size of a pea can be felt in the axillary space.

Dec. 15, 1915. Second radiation with the radium cannon. Application made in the same manner as before for thirteen hours. The dose is 76 e.

Feb. 15, 1916. The retraction of the nipple has lessened. The tumor cannot be palpated any more. Mamma freely movable upon the underlying tissues. The glandular nodes of the same hardness and the size of a pea are still palpable.

Aug. 2, 1916. Examination shows the same findings as Feb. 15. The glands in the axilla have disappeared.

tance 30 cm., size of field 14 x 14 cm. The dose applied was 160 e.

Dec. 8, 1915. The tumor has receded to the size of a cherry.

Dec. 11, 1915. Radiation with X-rays filtered with 1 mm. copper from a Coolidge tube, focus skin distance 50 cm., size of field 16 x 26 cm. Dose is 155 e.

Feb. 15, 1915. The growth, which at the last examination was the size of a cherry, is now palpable as an indefinite infiltration; it is no longer sharply circumscribed. Axillary and supraclavicular spaces are free.

Aug. 2, 1916. Same findings as on Feb. 15, 1916.

*From these observations we deduce that an essentially smaller dose measured with the aluminum chamber of gamma-rays of radium and mesothorium filtered with* 1.5 *mm. brass and* 5 *mm. celluloid is necessary than with X-rays filtered with* 1 *mm. copper to cause an essential resorption of a cancer node so it cannot any more be palpated.*

Additional observations of the same character made on one and the same person are not at our disposal, because it is rare to observe two cancer nodes of the same size in both breasts. However, we may draw upon a large number of clinical observations, in which we have used in one series of patients gamma-rays, in the other series X-rays for the resorption of cancer nodes in the breast.

*Radiation with gamma-rays of radium and mesothorium filtered with* 1.5 *mm. radium plus* 5 *mm. celluloid, by means of the radium cannon.*

*Case* 1. Mrs. G., 53 years old. Tumor of the right breast, just above the nipple, with broad base, size of a hen's egg. (Fig. 1, table XIII.) Histologic diagnosis of the pathological institute of Freiburg is carcinoma. Axillary and supraclavicular spaces are free.

*Day of first radiation:* Feb. 9, 1915. Duration, 12 hours. Dose applied, 70 e.

March 5, 1915. The tumor is reduced to about one-third the former size. General health good. Glands are not palpable.

*Second radiation:* March 21, 1915. Duration, 12 hours. Dose applied, 70 e.

*Radiation with X-rays filtered with* 1 *mm. copper.*

*Case* 2. Mrs. F., 48 years old. Clinical diagnosis: Carcinoma mammæ dextræ. Tumor size of a small fist, with broad base, but still movable. Extensive ulcerations on the surface. (Fig. 4, table XIII.) Two nodes, size of a walnut, are felt in the axillary region. Supraclavicular region is free. Histologic diagnosis of the pathological institute of Freiburg is carcinoma.

*Day of first radiation:* Aug. 17, 1915. Focus skin distance, 50 cm.; size of field, 20 x 20 cm. Dose, 165 e.

Sept. 20, 1915. Tumor reduced by one-half and encrusted on the surface. (Fig. 5, table XIII.)

*Second radiation:* Nov. 22, 1915. Focus skin distance, 50 cm. Size of field, 20 x 20 cm. Dose applied, 180 e.

April 24, 1915. Tumor is now the size of an almond and has crust formation. (Fig. 2, table XIII.)

*Third radiation:* May 11, 1915. Duration, 13 hours. Dose, 76 e.

July 7, 1915. The tumor has been reduced to the size of a hazelnut and is cicatrized. (Fig. 3, table XIII.) Axillary and supraclavicular spaces are free.

*Case* 3. Mrs. G., 52 years old. Carcinoma mammæ sinistræ. A tumor, size of a walnut, movable, is found above the left nipple. The mammilla is retracted. Glands cannot be palpated in the axillary and supraclavicular regions. Excision of tissue for examination. Histologic diagnosis of the pathologic institute of Freiburg is carcinoma.

*Day of first radiation:* Feb. 15, 1915. Duration of radiation, 12 hours. Dose applied, 70 e.

March 20, 1915. The skin shows in the center of the radiated field a light follicular reddening. The tumor has become essentially smaller. General health is good.

*Second radiation:* March 21, 1915. Duration of radiation, 12 hours. Dose, 70 e.

April 26, 1915. Tumor has disappeared. Erythema almost healed. Supraclavicular and axillary regions free.

Oct. 10, 1916. Same findings as April 26, 1915.

*Case* 5. Mrs. Sch., 42 years old. A tumor, the size of a hen's egg; hard, movable, sharply defined, formed in the right breast near the nipple. Axillary and supraclavicular spaces are free. Examination of excised tissue reveals carcinoma.

*Day of first radiation:* Feb. 25, 1915. Duration of radiation, 12 hours. Dose, 70 e.

March 18, 1915. Tumor has disappeared completely. Skin is slightly reddened. Patient cannot state when the redness appeared.

*Second radiation:* March 18, 1915. Duration, 12 hours. Dose, 70 e.

April 26, 1915. No erythema. Tumor not any more palpable. Axillary and supraclavicular spaces free.

*Case* 7. Mrs. E., 48 years old. Carcinoma mammæ sinistræ. The left nipple is somewhat retracted. A tumor, about the size of a hen's egg, freely movable, is felt underneath the nipple. Surface is irregular. Supraclavicular and axillary regions are

Feb. 4, 1916. Tumor has been reduced to a cortical induration the size of a nickel; the rest is covered with new, tender skin.

*Third radiation:* Feb. 3, 1916. Focus skin distance, 40 cm.; size of field, 20 x 20 cm. Dose applied, 135 e.

May 4, 1916. The crust has fallen off. New regenerated skin is found in place of the cancer. It is of a clear white. (Fig. 6, table XIII.)

Sept. 4, 1916. Same findings as on May 4th, only the skin has become somewhat harder.

*Case* 4. Mrs. D., 59 years old. A hard tumor, size of a child's fist, is felt in the outer half of the left breast. Axillary and supraclavicular spaces are free. Excision of tissue for examination. Histologic diagnosis by pathologic institute of Freiburg, carcinoma.

*Day of first radiation:* Feb. 24, 1916. Focus skin distance, 50 cm.; size of field, 20 x 20 cm. Dose, 160 e.

April 27, 1916. Tumor cannot be palpated any more; skin tanned; no erythema.

*Second radiation:* April 27, 1916. Focus skin distance, 50 cm. Size of field, 20 x 20 cm. Dose, 165 e.

Sept. 13, 1916. General health good. Axillary and supraclavicular regions are free. A small area of induration can still be felt.

*Case* 6. Mrs. M., 47 years old. Carcinoma mammæ dextræ. A tumor, size of a hen's egg, movable, formed in right breast. Axillary and supraclavicular regions are free. Histologic examination of excised piece of tissue reveals carcinoma.

*Day of radiation:* May 7, 1916. Focus skin distance, 50 cm. Size of field, 20 x 20 cm. Dose, 165 e.

Aug. 12, 1916. Tumor has completely disappeared. Axilla and supraclavicular space are free.

*Case* 8. Miss D., 51 years old. Carcinoma mammæ dextræ. Several nodes, varying in size from a pea to a plum, are found in the upper half of the breast. Excision of tissue for histologic examination reveals carcinoma.

free. Histologic examination of excised tissue reveals carcinoma.

*Day of radiation:* May 5, 1915. Duration of radiation, 12 hours. Dose, 70 e.

April 9, 1915. Erythema of first degree next to the nipple, size of a small dish-plate. No scaling of skin. Tumor cannot be palpated any more. Supraclavicular and axillary regions free.

*Case* 9. Miss D., 50 years old. Carcinoma mammæ dextræ. Tumor, size of a walnut, palpable in lateral half of right breast. It is freely movable. Axillary and supra-clavicular regions are free. Histologic examination of excised tissue reveals carcinoma.

*Day of first radiation:* April 14, 1915. Duration of radiation, 12 hours. Dose, 70 e.

June 5, 1916. Slight erythema, appearing five weeks after radiation. Tumor reduced one-third. Axillary and supraclavicular regions are free.

*Second radiation:* June 5, 1915. Duration, thirteen hours. Dose, 76 e.

July 30, 1915. Tumor has completely disappeared.

Aug. 22, 1916. General health good. Tumor gone; axillary and supra-clavicular regions free.

*Case* 11. Miss M., 62 years old. Carcinoma mammæ sinistræ. A firm induration, size of a 50-cent piece, freely movable, located to the left and above the nipple in the left breast. Axillary space is free. A gland, size of a hazelnut, palpable in supra-clavicular region. Histologic examination of excised tissue reveals carcinoma.

*Day of first radiation:* June 26, 1915. Duration of radiation, twelve hours. Dose, 70 e.

July 9, 1915. Erythema of first degree of a diameter of 10 cm. at the inner half of breast. Tumor is somewhat smaller. No pain on pressure.

*Second radiation:* July 27, 1915. Duration of radiation, thirteen hours. Dose, 76 e.

Sept. 20, 1915. An indurated area, size of a quarter, felt above the nipple in left breast. It is not sensitive to pressure. The upper layer of the skin was blistered, but has healed in the meantime.

*Third radiation:* Sept. 23, 1915. Duration, thirteen hours. Dose, 76 e.

May 26, 1916. An induration size of a nickel still felt. Skin had been somewhat irritated.

Oct. 5, 1916. General health good. A small area of induration still felt in the scar. Axillary and supra-clavicular regions are free.

*Day of radiation:* June 5, 1916. Focus skin distance, 50 cm.; size of field, 20 x 20 cm. Dose, 165 e.

Sept. 22, 1816. General health good. Tumor has completely disappeared.

*Case* 10. Miss G., 46 years old. Carcinoma mammæ sinistræ. Tumor, size of an apple, in left upper quadrant. Freely movable. Axillary and supraclavicular regions are free. Histologic examination of excised tissue reveals carcinoma.

*Day of radiation:* July 17, 1916. Focus skin distance, 35 cm. Dose, 165 e.

Sept. 19, 1916. Tumor has completely disappeared. Axillary and supraclavicular spaces are free.

*Case* 12. Miss Oe., 37 years old. Carcinoma mammæ sinistræ. A tumor, between size of a pigeon's and a hen's egg, found in the external upper quadrant of left breast, adherent to skin. Tumor is freely movable. Axillary and supra-clavicular regions are free. Histologic examination of excised tissue reveals carcinoma.

*Day of radiation:* July 19, 1916. Focus skin distance, 40 cm.; size of field, 18 x 18 cm. Dose, 165 e.

Sept. 20, 1916. Tumor is not any more palpable. General health good. Axillary and supra-clavicular regions are free.

*If we combine the results of all these cases we arrive at the same result as previously. To attain a resorption of a carcinoma nodule so it will disappear to the sense of touch, an essentially smaller dose of gamma-rays of radium and mesothorium, filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid, is necessary than of X-rays filtered with* 1 *mm. copper.*

## Comparative Observations on the Intensity of the Biologic Action of Differently Hard Rays on the Ovary

The third tissue variety, in which we could carry out a comparison of the intensity of the biologic action of the different hardness of rays, is the ovary.

The treatment of myomata and hemorrhagic metropathies with X-rays or gamma-rays of radium and mesothorium, has for its purpose the application of such a dose to the ovaries of the patients that a permanent amenorrhea results. The exact determination of this dose, which we will term *ovarian dose,* was impossible as long as one exclusively confined himself in the therapeutic radiation to the determination of the dose applied on the abdominal or sacral skin by the multiple small field method, then in general use. This dose was usually gauged with the Kienböck dosimeter. It, of course, does not tell us anything about the dose which arrived at the ovary of the patient. The dosation was rendered the more uncertain as one did not radiate in one sitting, but usually applied several series with an interval of about three weeks between the series. Some authors, as M. Fränkel, attempted to attain an approximate idea of the dose applied to the ovary by inserting Kienböck strips into the vagina. However, these attempts failed due to the uncertainty and deficiency of the dosation method.

We have endeavored to work out a more exact method of dosation and found in the ionization method the procedure which answered the requirements in every respect.

To measure the dose applied to the ovary, we inserted the ionization chamber—we used here also the aluminum chamber—under guidance of the palpating finger sufficiently high up into the rectum so that the chamber was placed beside and at the height of the palpable ovary. If the posterior vaginal wall was sufficiently deep, we inserted the ionization chamber in the posterior vaginal fornix. The measurement only then gave the exact ovarian dose, if the tumor was not too large, and if by palpation we could locate the ovary next to the chamber.

We have attempted to lessen the inexactness of dosation in the larger myomatous tumors, in which we could not exactly determine by palpation the position of the ovary to the chamber by choosing the distance of the focus from the ionization chamber as large as possible. For the greater the distance of the source of the X-ray

radiation from the ionization chamber, the less will the inexactness of the localization of the ovary give rise to errors in the determination of the dose. Further the determination of the ovarian dose was only then free from any objections if we attained amenorrhea in a single sitting. For, if we distributed the dose to several sittings at more or less long time intervals, the unknown action of the interval dose would be of real importance on the size of the dose.

That method of determination of the dose appeared to be the best with which we applied the dose to the ovary through a single port of entry. This was possible only then if the quotient of the dose, which

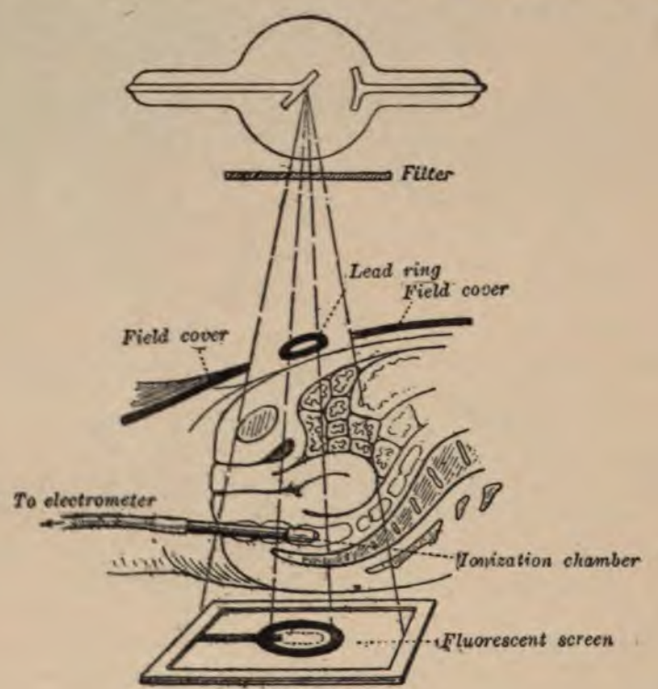



Fig. 47.

is dependent on the hardness of the rays, the focus skin distance and the size of the field, was sufficiently favorable.

We succeeded in these individuals to obtain a sufficiently favorable quotient of dose with a focus skin distance of 50 cm. and also with X-rays filtered with 3 mm. aluminum. In stouter individuals a stronger filtration with 10 mm. aluminum or 1 mm. copper was necessary. To render it certain that both ovaries and the ionization chamber were placed within the radiation beam, the location of the ionization chamber within the radiation beam was determined by means of the fluorescent screen before each radiation in the following manner: The location of the ionization chamber was vertically projected on the skin of the patient, who was lying in a horizontal position. At this place of the skin a lead ring was placed. By means

of the fluorescent screen placed beneath the patient it was ascertained whether the ionization chamber would throw a shadow in the middle of the lead ring.

Fig. 47 represents a median longitudinal section to show the procedure of placing the ionization chamber. The radiation was continued until the iontoquantimeter indicated the ovarian dose.

If we really intended to make comparative observations on the biologic action of the various kinds of rays it would have been necessary to ray one ovary with one quality of ray and the other ovary with another quality of ray in one and the same patient. It is self-evident that this is impossible as it is well-known that the remaining ovary will assume completely the function of the other ovary which had been destroyed. Therefore, we can never obtain a correct interpretation of the degree of functional activity of one ovary.

We must choose the way we adopted in the observations on the carcinoma and the erythema doses, that is, we must statistically collect a large number of cases to render the individual error as small as possible. We used as standards the cases treated with X-rays filtered with 1 mm. copper, and compared with it the cases treated with X-rays filtered with 3 mm. aluminum.

We also have attempted to include in these comparative observations the gamma-rays. Though we obtained amenorrhea after gamma radiations through the abdominal walls, a proof that the ovaries had received the ovarian dose, the measurement of the dose used in the method of roentgen radiations proved too inexact to enable one to draw final conclusions. The radiation field of the radium cannon is too unhomogeneous in spite of a most careful distribution of the various preparations, so that the difference in distances, between the position of the dosimeter chamber and the actual location of the ovaries must never be overlooked, as we may do with impunity in the cases radiated with heavily filtered X-rays in which we use large focus skin distances. Hence differences of a few centimeters are not of any significance in the dosation of filtered X-rays.

Before we communicate these observations, we must decide whether the ovaries are at all adapted as test objects for comparative investigations on the intensity of the biologic action of the various hardnesses of rays.

We already have mentioned, in the discussion of the skin as test object, that an organ can only then be used as a comparative test object if:

1. The same reaction as a result of the radiation can be proved in the organs.
2. The individual deviations with the use of the same dose must not be too large.
3. The sensitiveness must not descend below a certain definite value.

The occurrence of amenorrhea may be considered as a biologic

action in the ovaries of the rays, for X-rays as well as for the gamma-rays of radium and mesothorium.

The conditions in the ovary are unfortunately not the same as in the skin where we may judge of the intensity of the biologic action of a known dose from the intensity of the erythema. The expectation unfortunately is not fulfilled that in the ovary the greater or lesser intensity of the reaction is observable in an earlier or later occurrence of the amenorrhea. As our clinical observations show, the time of the occurrence of amenorrhea is quite independent of the size of the dose.

We have only two values in the ovary as a sign of the biologic action, the occurrence or non-occurrence of amenorrhea. Therefore the ovary is less suited for a valuation of the intensity of a biologic action than the skin. However, the ovary in comparison to the skin has the advantage of possessing fewer individual deviations toward the reaction of radiations.

We saw that the erythema dose of the skin differs according to the location of the skin area. The skin of the abdomen has a different erythema dose as the skin of the back. The skin of the perineum, as it is usually somewhat moist, has another erythema dose as the skin of the abdomen. Differences in age also play a certain rôle in skin reactions. These differences in the ability to react are less marked in the ovary.

The age of the patient, which ought to demand chief consideration in our observation, does not play any recognizable influence on the reaction. For differences in ages of twenty years within the period of sexual activity do not have any essential influence on the ovarian dose.

If other authors, contrary to these observations, accentuate the factor age, it must be stated that they determined the dose on the skin and not at the seat of the ovaries. They drew the conclusion for the therapeutic effect from the skin dose, without knowing the ovarian dose.

The sensitiveness of the ovary also is sufficiently great. Skin and ovaries are of about the same value as test objects, as we may conclude from the following observations.

When we began to bring about retrogression of myomata and hemorrhagic metropathies by obtaining amenorrhea in one sitting, we at first applied a relatively high dose to avoid failures. After we saw that amenorrhea appeared we changed to smaller doses until we finally reached the value of the smallest acting dose.

Altogether we have at our disposition over two hundred observations of myomata and hemorrhagic metropathies.

Mitscherlich was able to prove from the material of our clinic that the value of the smallest acting dose is relatively sharply definable.

All those patients became amenorrhoic that received an ovarian

dose of 33 e to 44 e. The first failures, that is, non-occurrence of amenorrhea, resulted from a dose lower than 33 e. The failures were already numerous with a dose of 23 e.

The sensitiveness of the ovary is therefore sufficiently large and we may use the ovary as a test object for observations on the intensity of the biologic action of various hard rays.

## Comparative Observations on the Intensity of the Biologic Action of X-Rays Filtered with 3 mm. Aluminum and 1 mm. Copper on the Ovary After Passing Through a Layer of Tissue Between Filter and Ovary

In the radiation of an ovary through a field on the anterior addominal wall the X-rays must first pass a layer of tissue of about 5 to 10 cm. before they reach the ovary. We proved in the physical part that X-rays filtered with 1 mm. copper do not essentially change their composition, if they penetrate a layer of tissue of a thickness of 5 to 10 cm. On the other hand X-rays filtered with 3 mm. aluminum do essentially change their composition depending on the thickness of the tissue layer penetrated. We therefore cannot compare the X-rays filtered with 1 mm. copper with the X-rays filtered with 3 mm. aluminum as we had done in our earlier observations, but we may gather from these observations whether with the same dose the biologic action of the various hard rays within the limits of 3 mm. aluminum and 1 mm. copper filtration is of different intensities.

The value of the smallest active ovarian dose was placed at 33 e and it was found from observation of cases that were radiated with 1 mm. copper.

We, therefore applied in lean individuals, in which the quotient of the dose permitted it, the same dose of X-rays filtered with 3 mm. aluminum to the ovary as in others with the use of X-rays filtered with 1 mm. copper. We possess ten such observations. They show that the dose applied to the ovary to produce amenorrhea is not higher when X-rays filtered with 3 mm. aluminum are used than with X-rays filtered with 1 mm. copper.

*It follows from these observations that amenorrhea occurs with about the same dose obtained with X-rays filtered with* 1 *mm. copper and X-rays filtered with* 3 *mm. aluminum. The intensity of the biologic action of X-rays filtered with* 3 *mm. aluminum or* 1 *mm. copper on the ovary after penetration of a layer of tissue between filter and ovary is about the same.*

It appears to be of interest to mention an analogous experiment in animals. The test object used was the frog larvæ. They were radiated beneath a layer of water 5 cm. thick analogous to the position of the ovary beneath the skin surface. Water, as has been demonstrated, may be considered of even value as human tissue concerning absorbability of rays and production of secondary radiations.

## Comparative Investigations on the Intensity of the Biologic Action of X-rays Filtered with 3 mm. Aluminum or 1 mm. Copper in the Larvæ of Frogs After Penetration of a Layer of Water 5 cm. Thick Between Filter and Larvæ

The details of the experiment correspond to those employed in the earlier tests with the difference that the larvæ were placed 5 cm. beneath the surface of the water. The measuring chamber also was placed at the same location. (See Fig. 42.)

*Course of the Experiment.*—The spawn clump from a pair of rana esculenta served as observation material. The eggs had so far developed that the embryos had assumed a bean shape within the membranes.

The observation material was divided into three parts, each of thirty eggs. Parts 1 and 2 were radiated, part 3 served as control. Part 1 was radiated with X-rays filtered with 3 mm. aluminum, and part 2 with X-rays filtered with 1 mm. copper.

The doses applied were 125 e at 5 cm. depth and obtained within 117 and 138 minutes respectively.

*Extract from the observation journal. Day of radiation:* June 26, 1915.

*Days of observation:*

June 28th—The animals have left the membranes. The controls are alive and of normal development. The radiated animals begin to show the characteristic symptoms of radiation disease. Differences between the two radiated groups cannot be recognized.

June 30th—The controls are alive and of normal development. The radiated groups almost all show the characteristic symptoms of radiation disease. The symptoms are generally much more marked in the animals of group 2 than in those of group 1.

July 2nd—One of the controls has died; the others are of normal development. Of group 2, three animals succumbed with the characteristic radiation symptoms. Otherwise, the same findings prevail as on June 30th.

July 5th—The controls are all alive and of normal development. Of group 2, twelve animals died; none of group 1.

July 7th—Twenty-five animals of the controls are still alive and of normal development. Two animals of group 2 are still alive. They show the characteristic radiation symptoms. All the animals of group 1 have distinctly marked radiation symptoms.

July 10th—The controls are all alive and of normal development. Two animals of group 1 are still alive.

*This experiment shows that the intensity of the biologic action of X-rays filtered with 3 mm. aluminum after penetration of a layer of water 5 cm. thick, is about the same as that of X-rays filtered with 1 mm. copper, if the dose has been determined with the aluminum chamber.*

## The Significance of the Dosimeter in the Determination of the Biologic Factor

In the preceding experiments we made use of our dosimeter and an ionization chamber in which electrodes and walls were constructed of aluminum in the determination of the dependence of the biologic factor on the hardness of the rays with like doses.

The experiments revealed the result that a dependence of the intensity of biologic action on the hardness of the rays exist. This difference in the intensity of the biologic action was not considerable with the differently filtered X-rays, however a very considerable difference prevailed between the intensity of the biologic action of the gamma-rays of radium and mesothorium and those of X-rays filtered with 1 mm. copper.

In the physical part and in the first paragraph of the biologic part we have already referred to the fact that a source of error was caused by the employment of aluminum as electrodes and chamber walls in the comparative dosimetry of the various hard rays and that an ionization chamber constructed of graphite electrode and walls was devoid of these errors. In biologic experiments, therefore, the results obtained with an aluminum chamber as a dosimeter can be valued correctly then when the error has been taken in account by gauging the results with a graphite chamber. The standardization between the aluminum chamber used in the experiments and the graphite chamber revealed that the aluminum chamber in comparison to the graphite chamber would indicate a dose the smaller the softer the employed radiation was. The difference was not very considerable, if roentgen rays were concerned, whether they were unfiltered or filtered with variously strong filters. On the other hand, it was very considerable if a comparison was made between X-rays and gamma-rays of radium and mesothorium filtered with 1.5 mm. brass plus 5 mm. celluloid.

In the following table the results with 1 mm. copper measured with the aluminum chamber correspond exactly to those obtained with the graphite chamber. With X-rays filtered with 10 mm. aluminum the dose measured with the aluminum chamber corresponds to only 0.86 of that measured with the graphite chamber; with X-rays filtered with 3 mm. aluminum the dose obtained with the aluminum chamber corresponds to only 0.81 measured with the graphite chamber. With unfiltered rays the dose measured with the aluminum chamber equals the dose measured with the graphite chamber. With gamma-rays of radium the dose measured with the aluminum chamber equals 2.27 of that measured with the graphite chamber.

| Hardness of rays | $h_1$ | Discharge time of aluminum chamber | Discharge time of graphite chamber | Ratio of discharge times | f |
|---|---|---|---|---|---|
| Unfiltered X-rays ..... | 2.2 | 2.1′ | 4.9′ | 2.33 | 1.00 |
| X-rays filtered with 3 mm. aluminum ..... | 4.3 | 2.14′ | 6.2′ | 2.9 | 0.81 |
| X-rays filtered with 10 mm. aluminum ..... | 6.9 | 4.75′ | 13.0′ | 2.74 | 0.86 |
| X-rays filtered with 1 mm. cu... | 10.5 | 3.5′ | 8.2′ | 2.34 | 1.00 |
| Gamma-rays ..... | 50 | 66′ | 68′ | 1.03 | 2.27 |

Let us now study with regard to the latter deductions the results which we have found in the comparison of the intensity of the biologic action of the rays of various hardnesses.

In the comparison of the intensity of the biologic action of unfiltered X-rays and of X-rays filtered with 1 mm. copper we saw that a difference in the intensity of the biologic action with like dose, measured with the aluminum chamber did not exist. In accordance with the table given above a correction of the dose does not have to be made with these qualities of rays. We therefore may omit in our results the restriction "measured with the aluminum chamber" and state the results thus:

*The intensity of the biologic action between unfiltered X-rays and X-rays filtered with* 1 *mm. copper is with like dose the same.*

In the comparison of the intensity of the biologic action of X-rays filtered with 3 mm. aluminum and of X-rays filtered with 1 mm. copper we found a recognizable difference in the intensity of the biologic action, if we measured the dose with the aluminum chamber. We placed the biologic factor at 0.75. According to the table we must make a correction, for the animals radiated with 3 mm. aluminum did not receive the same dose as those rayed with 1 mm. copper. This dose was 20 per cent lower. If we had applied to the animals radiated with 3 mm. aluminum a dose about 20 per cent higher in order to obtain a correct comparison of the biologic action with like dose, then the difference would have been so far annulled that a difference in the biologic action could not have been observed. The corrected result must therefore be expressed as follows:

*The intensity of the biologic action of X-rays filtered with* 3 *mm. aluminum and* 1 *mm. copper is with like doses the same.*

We found in the comparison of the intensity of the biologic action between gamma-rays of radium and mesothorium filtered with 1.5 mm. brass plus 5 mm. celluloid and X-rays filtered with 1 mm. copper, if we measured the dose with the aluminum chamber, an essentially stronger biologic action of the gamma-rays. According to the table we must here also apply a correction, because the animals rayed with gamma-rays did not receive the same dose as the animals radiated with X-rays filtered with 1 mm. copper, but a dose about 2.27 times larger. The difference in the intensity of the biologic action between these two radiations therefore is essentially smaller.

In the determination of the biologic factor we had applied to the animals radiated with X-rays filtered with 1 mm. copper a dose measured with the aluminum chamber three times larger than that applied to the animals radiated with gamma-rays, to establish the same intensity of the biologic action.

If we apply the correction according to the table then the difference of the applied dose is not 300 but only 20 per cent. The difference of 20 per cent cannot be expressed in the biologic results. The experiments made by us therefore permit the conclusion:

*A difference in the intensity of the biologic action between gamma-rays and X-rays filtered with* 1 *mm. copper must be small, if it*

*exists at all, for it cannot be recognized with a difference in dose of 20 per cent.*

Yet we deemed it desirable to perform a series of experiments with the same doses. We employed as test object the larvæ of rana esculenta. The details of the experiments were the same as those observed in the earlier biologic investigations with frog larvæ.

*Course of the Experiment.*—The spawn clump of a pair of rana esculenta served as observation material. The embryos had developed the medullary depression within the membranes. (See table XIV, Fig. 1.) They were divided into three parts, each of about fifty larvæ. One part was radiated with gamma-rays filtered with 1.5 mm. brass plus 5 mm. celluloid, the other with X-rays filtered with 1 mm. copper, while the third part served as controls.

The graphite chamber was employed as dosimeter chamber. The dose was in both instances 80 e. As the radiation with the gamma-rays required a longer time than the radiation with X-rays and to avoid errors, the application with the X-rays was undertaken in the middle of the time period that was necessary for the radiation with gamma-rays. After the radiation the larvæ were reared in the customary way in culture plates filled with pond water.

*Extract from the observation journal.*

*Day of radiation:* April 28.

*Days of observation:*

May 4th—The larvæ execute the first movements within the membranes. In some of the radiated animals the symptons of radiation disease have already appeared.

May 8th—The larvæ have left the membranes and swim about in the culture plates. Most of the radiated animals show the characteristic symptoms of radiation disease in the form of deformities and vesicular swellings. (Fig. 2, table XIV.) A difference in the degree of the symptoms between the groups of the radiated animals cannot be observed.

May 13th—The controls are all alive and of normal development. About half of the animals in each of the radiated groups have died; the rest show distinctly pronounced radiation symptoms. A difference between the groups of the radiated animals can also not now be observed.

May 18th—The controls are all alive and of normal development. The animals radiated with gamma-rays are all dead; the animals radiated with X-rays had succumbed by May 17th.

In the following table the number of living animals and the number of those showing radiation symptoms have been entered.

| Day of observation after radiation | Number of living control animals | Gamma-rays | | X-rays | |
|---|---|---|---|---|---|
| | | Number of living animals | Number of animals with radiation symptoms | Number of living animals | Number of animals with radiation symptoms |
| 6th day | 53 | 51 | 4 | 55 | 4 |
| 9th " | 53 | 51 | 12 | 55 | 14 |
| 11th " | 53 | 51 | 40 | 54 | 39 |
| 13th " | 53 | 51 | 44 | 53 | 43 |
| 14th " | 53 | 45 | 45 | 49 | 49 |
| 15th " | 53 | 27 | 27 | 26 | 26 |
| 18th " | 53 | 17 | 17 | — | — |
| 20th " | 53 | — | — | — | — |

*From these results we deduce: The intensity of the biologic action of gamma-rays of radium and mesothorium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid and X-rays filtered with* 1 *mm. copper is the same with the same dose.*

Since the intensity of the biologic action of unfiltered rays, and of X-rays filtered with 3 mm. aluminum and 1 mm. copper with like dose was the same, we may answer the question, "whether with the same dose the intensity of the biologic action of X-rays and gamma-rays is dependable on the hardness of the rays" thus:

*Within the limits of hardnesses of the radiations investigated the intensity of the biologic action is independent of the hardness of rays; the intensity of the biologic action is only dependent on the radiation energy absorbed.*

We have recorded the investigations of the dependence of the intensity of the biologic action on the hardness as they were gradually worked out in our laboratory. We intentionally reported the biologic results obtained with the aluminum chamber, though they required correction,—yes, were even misleading.

In the writings on the investigation of the dependence of the biologic action from the X-rays and gamma-rays of a known hardness with the same dose, as they have been published by various authors, the results obtained differ very essentially. Some find a marked dependence of the biologic action from the hardness, others take the view that the biologic action is only dependent on the absorbed X-ray energy. According to our investigations it is deemed very probable that the differences in the results of these writers are caused by the use of other dosimeters.

To again demonstrate the dependence of biologic results from the dosimeter we have made additional investigations on another test object, namely, the genus of vicea fava, which is used with preference by many authors in their investigations. In one series we have used the aluminum chamber and in the other we employed the graphite chamber. In both series the same doses measured with these chambers were applied.

The preliminary experiments showed that the garden beans are generally not as well adapted to comparative biologic tests as the frog spawn, because the sensitiveness of the vicea fava is a smaller one than that of the frog spawn. The latter already shows a pronounced difference in the biologic action if the dose varies 50 per cent, while a difference in the germinating garden bean is just recognizable with a difference in dose of about 100 per cent.

We expected, à priori, that on account of this relatively great insensitiveness differences in the biologic action of the differently hard X-rays could not be obtained when using both measuring chambers. We, therefore, employed the gamma-rays of radium and mesothorium filtered with 1.5 mm. brass plus 5 mm. celluloid for comparison with X-rays filtered with 1 mm. copper, because with these the

influence of the dose could be shown in spite of the relatively great insensitiveness of the test object.

The details of the experiment closely adhere to those observed in the biologic experiments with frog spawn, as shown in Figs. 42 and 43. The germinating garden beans were used in place of the frog larvæ. The measuring of dose was performed in the same manner.

*Course of the Experiment.*—From the harvest of the previous year of vicea flava, which descended from one family, a large number were placed at our disposal by the Botanic Institute of Freiburg. They were set in a closed culture plate lined with moistened blotting paper and kept in a warm room to germinate. Those beans were taken out after a few days in which sprouts of the same length and same thickness had grown out from the beans. The length of the sprouts averaged 2–3 mm. (See tables XV and XVI, Fig. 1.) Two groups of thirty beans each were subjected to radiations, while a third group of thirty beans served as control. A dose of 55 e was applied to one group with X-rays filtered with 1 mm. copper, and to another with gamma-rays from radium and mesothorium filtered with 1.5 mm. brass plus 5 mm. celluloid. The two dosimeters, one supplied with an aluminum chamber and the other with a graphite chamber, were so standardized that the doses from a radiation of X-rays filtered with 1 mm. copper were the same if measured with both instruments.

To obtain the same dose with gamma-rays, then with X-rays, a longer time of radiation is necessary with the gamma radiation. To avoid any error arising from the difference in the stage of development of the radiated beans, the radiation with X-rays was placed at the middle of the time of the gamma radiation. After radiation the radiated beans and controls were planted equally deep in beds filled with humus best suited for a good growth and kept at even temperature in the greenhouse of the botanic institute. After the sprouts had grown out from the ground they were photographed at intervals of eight days.

### *Extract from the observation journal.*

*Dosation with the Aluminum Chamber.*
*Days of radiation:* Dec. 5, 1916.
*Days of observation:*

Dec. 9, 1916. Some of the controls have sprouted out above the ground, while sprouts cannot be seen in the radiated beans.

Dec. 13, 1916. The radiated beans as well as the controls have thrown out shoots above the ground. However, the radiated beans in comparison to the controls show marked retardation in growth, which is much more pronounced in the plants radiated with gamma-rays than in those radiated with X-rays.

Dec. 20, 1916. The plants show a progressive and vigorous development. The dif-

*Dosation with the Graphite Chamber.*
*Days of radiation:* Dec. 14, 1916.
*Days of observation:*

Dec. 18, 1916. Some of the controls have already sprouted out above the ground. The radiated beans do not show any sprouts.

Dec. 21, 1916. The radiated beans and the controls have thrown out sprouts above the ground. However, the radiated beans in comparison to the controls show marked retardation in growth, which is much more pronounced in the plants radiated with gamma-rays than in those radiated with X-rays.

Dec. 27, 1916. The plants show a progressive, vigorous development. A difference

ference in the intensity of the biologic action between the plants radiated with gamma-rays and those radiated with X-rays is very noticeable. A thickening of the leaf epithelium and an abnormal shape of the leaf are evidences of characteristic radiation symptoms. (Fig. 2, table XV.)

Dec. 27, 1916. The plants of all groups have continued to develop vigorously. A difference in the intensity of the biologic action of gamma-rays remains visible. (Fig. 3, table XV.) It appears that the plants in their further development slowly recover from the action of the radiation. The leaves grown last do no longer show a thickening of the epidermis.

in the intensity of the biologic action of gamma-rays and those of X-rays cannot be recognized (Fig. 2, table XVI). A thickening of the leaf epithelium and an abnormal shape of the leaf are seen as evidences of characteristic radiation symptoms.

Jan. 4, 1917. The plants in all groups have continued to grow vigorously. An influence of the radiation on the radiated plants remains further visible. A difference between the plants radiated with gamma-rays and those radiated with X-rays is not observable. (Fig. 3, table XV.)

From the two series of experiments the following conclusions may be drawn. The influence of the biologic action between gamma-rays of radium and mesothorium filtered with 1.5 mm. brass plus 5 mm. celluloid and X-rays filtered with 1 mm. copper is observable in the sprouts of vicea fava. If we apply with both radiations the same dose, measured with the aluminum chamber we see a difference in the intensity of the biologic action of both radiation varieties in the sense that the more intense biologic action must be attributed to the harder rays. On the other hand if we apply the same dose, measured with the graphite chamber, this difference in the intensity of the biologic action of both radiations disappears.

*Comparative Observations on the Intensity of the Biologic Action of Gamma-rays of Radium and of the Gamma-rays of Mesothorium filtered with* 1.5 *mm. Brass plus* 5 *mm. Celluloid.*

We have until now considered the filtered gamma-rays of radium and mesothorium always as rays of like hardness and always compared the intensity of the biologic action of a combination of these gamma-rays with that of filtered X-rays. We were compelled to do this because we had to use the entire supply of radium and mesothorium in the comparative biologic investigations on the influence of X-rays and gamma-rays on frog larvæ and because the total amount only sufficed to apply within a reasonable time to the frog larvæ the required measurable dose for the production of the radiation disease.

Physical investigations on the composition of the gamma-rays of radium and mesothorium revealed that a small difference in the composition of the rays is present. Though it was to be assumed, at the outset, that this small difference would not be expressed in the biologic reaction, we deemed it advisable to perform comparative investigations on the intensity of the biologic action of gamma-rays of radium and mesothorium, because in literature statements are found that a smaller biologic action must be attributed to the gamma-rays arising from radium than to those emitted from mesothorium.

As we could not compare with each other the gamma-rays of radium with those of mesothorium in their influence on beings of low life on account of an insufficient amount of radio-active substances, we confined our investigation to the human skin, because a method of dosation somewhat free of objections can then be used.

We employed a radium capsule and a mesothorium capsule for the comparative observations. The gamma-rays of the radium capsule had a gamma-ray activity of 48 mg. radium element and the gamma radiation from the mesothorium capsule had a gamma-ray activity of 47.7 mg. radium element. The gamma-ray measurement was performed according to the method given on page 10.

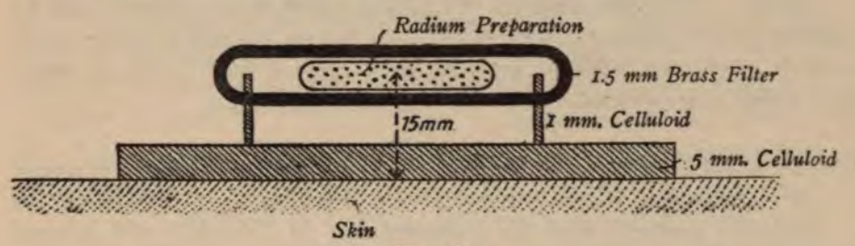



FIG. 48.

*Course of the Experiment.*—The radium or mesothorium capsule was placed in the center of a brass capsule of a wall thickness of 1.5 mm. as shown in natural size in Fig. 48. The brass capsule rested on a frame of celluloid of a thickness of 1 mm. which had a base of celluloid of a thickness of 5 mm. that extended over the capsule all around to arrest the secondary beta rays. This radiation applicator was filled at one time with mesothorium and at another time with radium and applied to skin surfaces that were as homogeneous as possible. The distance from the center of the preparation to the skin was 15 mm.

We may assume that with like distance from the skin, with like applicators and with the same time, the doses applied to the skin must be the same as the size and activity of both capsules were about the same.

*Extract from the observation journal.*

We made use of our skin for this experiment. The radium capsule was applied to the right infra-clavicular region, and the mesothorium capsule to the infra-clavicular region. The time duration of application for both preparations was fifty hours and lasted from Nov. 5, 1915, 5 P.M., to Nov. 7, 1915, 7 P.M.

| Field $a$ = radium | Field $b$ = mesothorium |
|---|---|
| Nov. 13, 1915: Distinct reddening appears. | Nov. 13, 1915: Reddening appears. |
| Nov. 17, 1915: Marked erythema of first degree. (Fig. 1, table XVII.) | Nov. 17, 1915: Marked erythema of first degree. (Fig. 2, table XVII.) |
| Nov. 24, 1915: Beginning of blister formation. | Nov. 24, 1915: Beginning of blister formation. |

| | |
|---|---|
| Nov. 30, 1915: Free secretion from the ruptured vesicle. | Nov. 30, 1915: Free secretion from the ruptured vesicle. |
| Dec. 2, 1915: In place of the blister a scab the size of a quarter. (Fig. 3, table XVII.) | Dec. 2, 1915: Scab, size of a dollar. (Fig. 4, table XVII.) |
| Dec. 10, 1915: Scab still present. (Fig. 5, table XVII.) | Dec. 10, 1915: Scab dropped off in center; beneath it freely secreting skin. (Fig. 6, table XVII.) |
| Dec. 15, 1915: Scab healing. (Fig. 7, table XVII.) | Dec. 15, 1915: Separation of scab is somewhat delayed in comparison to *a*. (Fig. 8, table XVII.) |
| Dec. 21, 1915: Scab has disappeared with the exception of a small remnant. Skin free of scars. (Fig. 9, table XVII.) | Dec. 21, 1915: Scab preserved for a somewhat longer period; new skin next to it. (Fig. 10, table XVII.) |

*Result: The intensity of the biologic action of gamma-rays of radium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid, is the same as that of gamma-rays of mesothorium filtered with* 1.5 *mm. brass plus* 5 *mm. celluloid with like dose and like intensities.*

*Comparative Observations on the Biologic Action between Beta-rays of Uranium-x after passing through a Layer of Aluminum as thin as possible and the Gamma-rays of Mesothorium filtered with* 1.5 *mm. Brass plus* 5 *mm. Celluloid.*

In the experiments made hitherto for comparison we have employed only the gamma-rays of radium and mesothorium. As is well known these substances send also out alpha- and beta-rays besides the gamma-rays. The alpha-rays are absorbed in the capsule holding the radio-active salt and cannot produce any reaction outside of the capsule. A large part of the beta-rays, however, penetrates the capsule, and we know from numerous observations, that a biologic action must be ascribed to these rays. So far systematic and exact investigations on the intensity and kind of the biologic action of beta-rays in comparison to the gamma-rays have not been available. The beta-rays of radium and mesothorium could not be used for comparative investigations because we can never recognize the biologic action of these beta-rays, as they are always mixed with a considerable proportion of gamma-rays. It is possible to isolate the gamma-rays from the beta-rays by physical methods, for instance, by a magnetic field. This method is too inconvenient, so it does not appear to be well suited for biologic test, especially on the skin. The customary test objects, frog spawn and beans, also cannot be employed on account of the difficulties of dosation with relatively weak preparations.

To study the biologic action of beta-rays without admixture of gamma-rays, we deemed proper the use of uranium-x as source of radiation, as in this preparation such a small amount of gamma-rays is present that the results of observation do not suffer an appreciable error according to our biologic experiences.

We used 5 Kg. of uranyl nitrate for the preparation of the nec-

essary amount of uranium-x, which was placed at our disposal by the chemical works of Merck in Darmstadt. We employed the method of absorption with animal charcoal so as to unnecessarily contaminate the residue with foreign chemicals, as the latter was to be used for other purposes. The 5 Kg. uranyl nitrate were dissolved in 40 liters of water. Ten grams of pure pulverized animal charcoal were added and the mixture uninterruptedly stirred for ten days by means of a paddle in a big glass trough. According to the investigations of A. Ritzel* the maximum of adsorption of uranium-x by the animal charcoal has occurred within this period. The solution was then left standing for a time so that the coal settled at the bottom. The clear fluid above the sediment was siphoned off. The residue with the animal charcoal content was filtered. The residue left behind on the filter was reduced to ashes and burned in a crucible. A residue of a few grams of a gray-brown powder was obtained which proved to possess a strong beta radiation when measured with an electroscope. Therefore it contained a large proportion of uranium-x.

As the action of uranium-x was to be compared with a mesothorium capsule, it became necessary to render the volume of the uranium-x preparation the same as the volume of the mesothorium preparation. A small platinum capsule of exactly the same dimensions as the mesothorium capsule served for the reception of the uranium-x. To reduce in volume the residue containing the uranium-x without decreasing its amount, the residue was treated with chemically pure hydrochloric acid of highest concentration. After a certain time of action of the hydrochloric acid, the non-soluble substances were separated by centrifugal force. This operation was repeated several times and the insoluble substances were finally washed with distilled water and filtered. The acid and the water were dried in a porcelain dish on a waterbath placed in the small platinum capsule above described and the hydrochloric acid finally driven off by red heat. A small residue was left in the platinum capsule, which contained mostly uranium-x.

As it was shown electrometrically that the undissolved residue possessed considerable activity, as much of the residue as possible was placed in the platinum capsule. The latter was sealed and placed in an aluminum capsule. The side of the capsule through which the beta-rays were to pass was of a thickness of 0.05 mm. The capsule thus prepared was used for the biologic experiments.

A measurement of the capsule with the beta-ray electroscope, made on the day of its completed manufacture, revealed that the activity was equivalent to a gamma-ray activity of about 5 mm. radium element.

The chief difficulty consisted in comparing biologically the beta radiation arising from this preparation with the gamma-rays. We

* A. Ritzel, Zeitschrift für physikalische Chemie, 67, 1909.

are dealing with two kinds of radiation which cannot be compared with each other because one radiation has a corpuscular character and the other the character of a ray wave. If we, in spite of this fact, compare the beta-rays with the gamma-rays we are perfectly conscious of the sources of errors attached to such a procedure.

The comparative dosation of both kinds of radiation with the ionization method appeared to us to be freest from any objections.

We employed for the measurement of both radiations the beta electroscope shown in Figs. 3 and 4. The gamma-rays were obtained from a mesothorium preparation filtered with 1.5 mm. brass plus 5 mm. celluloid. A brass filter surrounded the mesothorium capsule which was kept at a distance of 1 meter from the electroscope. The celluloid filter was placed directly against the aluminum wall of the electroscope because we were desirous to keep away from the electroscope not only the secondary radiations arising in the brass filter but also the secondary rays arising from the objects kept in the workroom. Only thus were we assured that the conditions during the measurement would equal those at the skin as closely as possible. In radiation applications to the skin the brass and celluloid filters are placed directly on the skin. Thereby the radiation field is protected from undesirable beta radiations.

To measure the beta-rays arising from the uranium-x preparation, the latter was kept at the same distance from the beta-ray electroscope as the mesothorium preparation, namely, 1 meter. It is self-evident that filters were not used.

It is well known that uranium-x has a half decay period of 24.6 days. Therefore the measurement for the determination of the dose had to be undertaken shortly before each biologic experiment. As the beta radiation activity of our uranium-x preparation was only of such an amount that according to preliminary tests an application of a duration of several days was necessary, the decrease in the activity during the period of radiation plays a rôle that cannot be overlooked. This decrease had to be considered in the final result if we desired to obtain a comparison with the gamma-rays of mesothorium. The methods of this calculation will not be described as they may be reviewed in textbooks on the decay of radio-active substances.

The examination was conducted as follows: Two homogeneous places of the infra-clavicular regions were radiated. The mesothorium capsule was applied to the left side. It was enclosed in a brass filter of 1.5 mm. The carrier was arranged as seen in Fig. 49. The capsule rested on a ring of hard rubber which was attached to a celluloid plate of a thickness of 5 mm. The plate extended beyond the hard rubber ring on all sides. The distance of the mesothorium capsule from the skin amounted to 1.5 cm. The uranium-x preparation was applied to the right side. It was mounted on a frame of the same construction. The brass filter and also celluloid were omitted within the area of the hard rubber ring, so that the beta-rays might strike

the skin directly. The distance of the uranium-x preparation from the skin was 1.5 cm. A measurement taken on the day of its application, Jan. 29, 1916, revealed that the uranium-x preparation possessed an activity equivalent to a gamma radiation of 4.43 mg. radium element.

The mesothorium capsule had a gamma-ray activity of 9 mg. radium element. It required a time duration of seventy-five hours to obtain a distinct erythema according to our experiences. The ura-

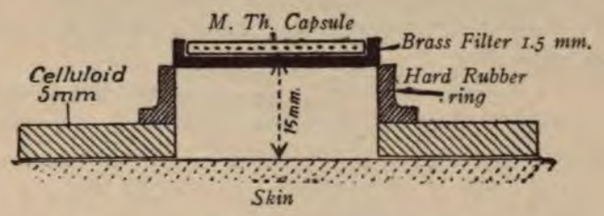



FIG. 49.

nium-x preparation, therefore, required a time duration of radiation of 152 hours including the loss due to the decrease of its activity to obtain the same dose.

*Extract from the observation journal.*

| Field *a*. Left infra-clavicular region. Mesothorium capsule. | Field *b*. Right infra-clavicular region. Uranium-x preparation. |
|---|---|
| *Days of radiation:* From Jan. 29, 1916, at 6 P.M., to Feb. 1, 1916, at 9 P.M. | *Days of radiation:* From Jan. 29, 1916, at 6 P.M., to Feb. 5, 1916, at 2 A.M. |
| *Days of observation:* | *Days of observation:* |
| Feb. 1, 1916: After removal of capsule a light reddish discoloration is seen which disappears after a day. | |
| Feb. 5, 1916, A.M.: Skin again normal. | Feb. 5, 1916: After removal of capsule a light reddening is seen. |
| Feb. 8, 1916: Slight brownish, yellowish discoloration. (Fig. 1, table XVIII.) | Feb. 8, 1916: Slight increase in the intensity of the erythema. At a few places superficial loss of skin. (Fig. 2, table XVIII.) |
| Feb. 17, 1916: Moderate reddening. At one place slight loss of epithelium of the most superficial epidermis. (Fig. 3, table XVIII.) | Feb. 17, 1916: Somewhat intense reddening. The loss of substance has not yet healed. (Fig. 4, table XVIII.) |
| Feb. 22, 1916: The erythema has increased in intensity; distinct formation of scab in center. (Fig. 5, table XVIII.) | Feb. 22, 1916: Erythema decreasing. Scale formation over the erosions. (Fig. 6, table XVIII.) |
| Feb. 25, 1916: Scab is slowly separated. (Fig. 7, table XVIII.) | Feb. 25, 1916: Progressive healing. (Fig. 8, table XVIII.) |
| March 3, 1916: Skin free of scars. | March 3, 1916: Skin free of scars. |

This observation was repeated with another preparation of uranium-x which was obtained after 3 months from the solution in which another additional portion of uranium-x had been formed in the meantime. The course of the experiment and the method of dosa-

tion remained the same. The results resembled the preceding one so closely that we will dispense with a repetition.

*Result.*

*From these experiments the following results are to be drawn:*

1. *A strong biologic action must be ascribed to the beta-rays in their action on the skin.*

2. *This biologic action resembles macroscopically in almost all points the biologic action of gamma radiation on the skin, with the only difference that the reaction appears somewhat earlier in radiations with beta-rays.*

3. *If we measure the beta- and gamma-rays according to the method described, the biologic action of gamma- and beta-rays on the skin surface is of the same intensity with like doses.*

The opinion has been frequently expressed that we must explain the biologic action of gamma-rays in the tissues as being not an indirect but a direct action. The process was usually interpreted as follows: A secondary radiation arises in the tissues when struck by gamma-rays and these corpuscular radiations call forth the biologic action. This assumption was rendered probable by the well-known experiments of the English investigator Wilson, who proved that the process of ionization may with great probability be ascribed to the secondary beta radiations caused by the X-rays when traversing air.

The close similarity in the biologic action of gamma-rays and beta-rays as determined in our experiment, may according to our opinion serve to support this view that the action of the gamma-rays in the tissues is an indirect process.

## Observations on the Dependence of the Intensity of the Biologic Action with Like Dose on the Intensity of the Rays

We understand by the applied radiation dose the product of the intensity of the rays and time divided by the half absorption value layer of the radiation, i.e., $\frac{J.\ t.}{h}$ It is evident that we may attain with the same hardness the same dose by applying a small intensity within a long time or a large intensity within a correspondingly short time. Of late in the construction of roentgen transformers special importance has been attached to the attainment of a high intensity, and one thought, based on clinical observations, to be able to obtain thereby a better biologic action and also an improvement in the economy. Clinical observations, however, as far as we could deduce from the literature, give a picture so at variance that it was impossible to draw uniform conclusions.

We therefore deemed it our duty to carry out special investigations on this point.

The relation between time and intensity in the action of light-rays on photographic plates has been an object for investigations for many years. These experiences have been expressed into laws, which were propounded by Schwarzschild in the *Schwarzschild law.* The observations proved that distinct differences in the action of light on photographic plates with a like amount of light result only from very great differences in the intensity and correspondingly very great differences in time. For fluctuations in intensity and time below these extremes the equation: J. t = const., was practically fulfilled. Therefore we had to determine by observation, on account of the common analogy between light and X- or gamma-rays, whether a similar law may be confirmed for the action of X- and gamma-rays on biologic objects.

Analogous experiments can only be performed with the use of the gamma-rays of radium and mesothorium because we are then dealing with a continuously glowing source of light just as with light-waves. To attain the same dose it is necessary to use a varying time duration of radiation when employing differently intensive ray sources. These variously long-time durations for all biologic objects harbor the source of error that the biologic object is not equally capable of reaction within differing periods of time. The error will be the larger, the greater the differences in time are, and the more the ability of the biologic object is to recuperate within these time periods. The organisms of low order, as frog spawn and sprouting garden beans used by us with preference as test objects in the biologic experiments, react already quite differently within small differences of time on account of their rapid development. Their use therefore must be excluded, as a dependence of the biologic action from the intensity can only be observed from the employment of intensity and corresponding differences in the time duration of the application.

The human skin appears to be the only usable and biologically comparable test object under like conditions within more or less marked differences in time. Certain limitations must be observed as the degree of the dryness of the skin and the homogeneity of the skin regions. The investigations on the dependence of the action of light on the intensity with like amount of light are not completely analogous to the experiments with X-rays, for the source of X-rays is not a continuous one, as the X-ray tube is operated with an intermittent electric current from an inductor or transformer and flashes up in intervals. Two ways are open to investigate on the skin the dependence of the biologic action from the intensity. In the first the Roentgen tube flashes up in equal intervals within a unit of time in the experiments in one instance with small intensities and in the other with large intensities. The intensity of the single flashes is of different strength and the same dose is obtained within different time durations. In the second way the dose is applied

with different intensities within the same time duration. The time intervals between single interruptions (which have different intensities) of the tubes vary in duration.

In the first instance the experiment will resemble those performed with light as nearly as possible. The same difficulties unfortunately are observed in the biologic object in these tests which we have just discussed in the gamma-rays, namely, within variously long time durations of radiations, the ability of the biologic object to react changes.

The second method does not adhere so closely to the experiments made on light, because in it not only the intensity but also the intervals between the different interruptions change. However, the method has the advantage of applicability in all biologic objects because the time durations of the radiations are equal.

Our experiments may be grouped as follows:

1. Comparative observations on the intensity of the biologic action of gamma-rays of radium and mesothorium with the same dose but different intensities.

2. Comparative observations on the intensity of the biologic action of filtered X-rays with equal dose, equal light intermissions but different intensity and time duration of radiation.

3. Comparative observation on the intensity of the biologic action of filtered X-rays of like dose, like time duration of radiation but different intensities and light intermissions.

*Comparative Investigations on the Intensity of the Biologic Action of Gamma-rays of Radium and Mesothorium on the Skin, with Like Dose but Different Intensities.*

We used two flat mesothorium capsules, which possessed a great difference of radiation energy in their activity. We equalized this difference in the intensity by means of different time durations of the radiations to obtain like doses. We fully recognized that certain differences in the dosation were unavoidable, though the measurement of the activity was performed with exactness. The difference resulted from the distribution of the radio-active salt in the capsules and the importance of the law of squares even when the same distance of the capsules from the skin was maintained. The gamma-ray activity of the capsules was 9 and 35.5 mg. radium element. The capsules had about the same length, a diameter of 27 mm., and a thickness of 4 mm.

Both capsules were contained in a cylindrical brass filter box of a wall thickness of 1.5 mm. See Fig. 48. It was mounted on a hard rubber ring, which was attached to a celluloid plate of a thickness of 5 mm. The celluloid extended over the hard rubber ring for 2 cm. all around. The distance of the mesothorium capsules from the skin was 15 mm.

*Course of the Observation.*—The observations were made on the

skin at two homogenously located regions of the right and left forearm. Field *a* was radiated with the capsule of 35.5 mg. radium element, field *b* with the capsule of 9 mg. radium element activity. The duration of the application to field *a* was 50 hours, that to field *b* was 200 hours.

To obtain like results in fields *a* and *b* for subsequent observations the time duration of the application of the 35.5 mg. capsule was arranged so that it fell within the middle of the total time duration of the radiation in field *b*.

*Extract from the observation journal.*

| Field a. | Field b. |
|---|---|
| *Beginning of radiation:* May 14, 1916, at 12.30 P.M., with 35.5 mg. Ra. el. mesothorium' capsule. | *Beginning of radiation:* May 11, 1916, at 9.30 A.M., with 9 mg. Ra. el. mesothorium capsule. |
| *End of radiation:* May 16, 1916, at 2.30 P.M. | *End of radiation:* May 19, 1916, at 5.30 P.M. |
| *Days of observation:* | *Days of observation:* |
| May 26: Diffuse reddening without formation of blister. (Fig. 1, table XIX.) | May 26: Diffuse reddening with distinct formation of vesicles in center. (Fig. 2, table XIX.) |
| May 29: Distinct blister formation in the center of the erythema. (Fig. 3, table XIX.) | May 29: The blister opened, beneath it new red skin. (Fig. 4, table XIX.) |
| June 2: Blister ruptured, new red skin in region of blister. Formation of scab with raised edges. (Fig. 5, table XIX.) | June 2: Beginning of formation of scab, which surrounds, wall-like, the new red skin. (Fig. 6, table XIX.) |
| June 9: Marked formation of scab and crust. (Fig. 7, table XIX.) | June 9: The crust has separated at a place to the right (Fig. 8, table XIX.) |
| July 7: The crust has been partly shed at one place, and partly reformed at another place. Distinct tendencies to heal. (Fig. 9, table XIX.) | July 7: Formation of new scabs which had been shed. The entire field has essentially decreased in size. (Fig. 10, table XIX.) |
| July 18: Scab is slightly adherent, beneath it distinct evidences of healing. (Fig. 11, table XIX.) | July 18: A crust, size of a dime, still remaining. Young red skin beneath the detached crust. (Fig. 12, table XIX.) |
| Last observation at the end of August. Healing without scar-formation. | Last observation at the end of August. Healing without scar-formation. |

*Result.*

*A dependence of the intensity of the biologic action is not recognizable within a difference of intensity of 1 : 4 of the rays. The same reaction occurs with the same dose.*

*Comparative Observations upon the Human Skin on the Intensity of the Biologic Action of Filtered X-Rays with the same Dose, same Light Intermissions but different Intensities and Time Durations of the Radiations.*

The observation was made at the time of the treatment of a patient suffering from an inoperable ovarian carcinoma. Two homogeneous skin regions of the abdomen, to the left and to the right of the median line, were used for the radiation. The radiation was performed in such a manner that the skin area *a* was treated

with low intensities of X-rays, and area *b* with intensities of X-rays as high as possible. The proportion of the intensities was obtained from the time duration within which the dose was achieved on the two fields. The time duration for field *a* amounted to 691 minutes, for field *b* 86 minutes. The filter consisted of 10 mm. aluminum. The dose was 230 e in both instances.

*Extract from the observation journal.*

| Field *a*. | Field *b*. |
|---|---|
| Radiation with low intensity. | Radiation with high intensity. |
| *Day of radiation:* Nov. 6, 1916. | *Day of radiation:* Nov. 6, 1916. |
| *Days of observation:* | *Days of observation:* |
| Dec. 4, 1916: Slight acne-like reddish discoloration in the radiation field. (Fig. 1, table XX.) | Dec. 4, 1916: Acne-like reddening more pronounced than in field *a*. (Fig. 2, table XX.) |
| Dec. 11, 1916: More confluent erythema of first degree. (Fig. 3, table XX.) | Dec. 11, 1916: Confluent erythema of first degree with isolated vesicle formation. (Fig. 4, table XX.) |
| Jan. 2, 1917: Erythema has disappeared; light browning of skin present. (Fig. 5, table XX.) | Jan. 2, 1917: The erythema begins to heal. The skin has been partly removed in small islands. The vesicles have partly dried up with the formation of scabs. (Fig. 6, table XX.) |

Three additional parallel observations are also at our disposal, which we will not record, as they revealed about the same results.

*Result.*

*Within a difference of intensity of* 1 : 8 *a dependence of the intensity of the biologic action on the intensity of the rays is recognizable with like doses. With like doses the stronger reaction takes place with the higher intensity.*

*Comparative Observations on the Intensity of the Biologic Action of Filtered X-rays with Like Dose, Like Light Intermissions but Different Intensities and Time Duration of the Radiations on the Human Ovary.*

The determination of the ovarian dose with a low limit of 33 e when radiating with X-rays rendered it possible to establish the importance of the intensity of the rays with like doses for the intensity of the biologic action on the ovary.

If we radiate a myoma through the abdominal wall with one field and place the ionization chamber at the ovary through the rectum, then the dose is attained, depending on the thickness of the overlying tissues in fat women within a longer time, and in lean women within a shorter time. The differences may be considerable and may be expressed in the proportions of the time durations of the radiations which may be as 1 : 4. The conditions therefore are similar to those on the skin, where we also determined the ratio

of the intensity of the rays from the differences in the time durations of the application of the rays.

We will report a few of the clinical histories. We shall group them so, that the cases are placed on the left side in which a high intensity of the rays, measured at the ovary, prevails; on the right side the cases in which a low intensity of rays, measured at the ovary, prevails.

Dose = 33 e.

Mrs. J., 50 years old. Uterus myomatosis. Uterus somewhat enlarged. Dose of 33 e is applied within 96 minutes. Amenorrhea after eight weeks. Uterus small.

Mrs. G., 53 years old. Uterus size of a small fist. Severe menorrhagias. The dose of 33 e is given within 184 minutes. Amenorrhea after ten days. Examination four months following radiation reveals a quite small, movable uterus.

Dose = 37 e.

Mrs. D., 41 years old. Uterus changed into a tumor size of a fist. Severe menorrhagias. The dose of 37 e is given within 117 minutes. Amenorrhea after five weeks. Examination after seven months: Tumor disappeared.

Mrs. R., 47 years old. Metropathy. Severe menorrhagias. The dose of 37 e is given within 90 minutes. Amenorrhea after six weeks.

Mrs. L., 38 years old. Myoma uteri. Tumor size of three fists. Dose of 37 e attained within 135 minutes. Amenorrhea after two months.

Mrs. B., 35 years old. Uterus size of a fist. The dose of 37 e is attained within 243 minutes. Amenorrhea after fourteen days. Examination after three months: Tumor completely gone.

Mrs. V., 50 years old. Uterus retroflexed. Metropathy. Severe menorrhagias. The dose of 37 e is given within 333 minutes. Amenorrhea after fourteen days.

Mrs. L., 49 years old. Tumor size of a man's head. The dose of 37 e is given within 342 minutes. Amenorrhea after two months. Examination after four months. Tumor size of a child's head.

*Result.*

*In the radiation of myomata and hemorrhagic metropathies the intensity of the biologic action on the ovary with like doses is independent from the intensity of the rays within the limits of 1 : 4.*

*Comparative Observations on the Intensity of the Biologic Action of Filtered X-Rays with Like Dose, Like Time Duration of Radiation but Different Intensities and Light Interruptions.*

Of the apparatus at our disposal for these comparative investigations, the Unipuls apparatus and the Apex instrumentarium of Reiniger, Gebbert and Schall appeared to be the most suitable.

The Unipuls apparatus enables one to produce single impulses of very high intensities by a corresponding change in the proportions of the primary and secondary wiring of the transformer and a proper interrupter. The interrupter had been exclusively constructed for diagnostic purposes, the delivery of a single impulse was executed by a manual manipulation. As many single impulses are necessary in therapy, the interrupter was connected with an electric motor. The number of the single impulses could thus be regulated within certain limits and was about 36 per minute.

The Roentgen-tubes used for diagnostic purposes for the unipuls snapshots are rather soft, so they can hardly be employed for therapeutic purposes with filtered X-rays.

The duration of the life of these tubes with long-continued therapeutic radiations is also a short one. We therefore employed the Coolidge tube and observed that it sufficed for our experiments. The temperature of the cathode could be increased by the filament current to such a degree that it took the high intensities of the current of the single impulses, and at the same time the desired hardness or potential at the terminals of the tube could also be easily attained.

This apparatus was employed for the radiations with high intensity and long light interruptions.

For the radiations with low intensity and short light interruptions the Apex instrumentarium with gas interrupter was employed. Here also a Coolidge tube of the same type was used.

The objection might be raised that our dosimeter would not permit to measure the dose in an unobjectionable manner because the apparati produce X-rays of such varying intensities. The saturation current might not be attained due to the great density of the ions in the ionization chamber produced by the single impulse. Investigations in this direction revealed that these sources of error did not obtain.

We performed the experiments on the frog spawn as biologic test object. We may use the latter in these experiments, because the dose is applied within the same time duration of the radiation.

The course of the experiment adhered closely to those used in our earlier biologic experiments. The same radiation stands and vessels were used. The filter consisted of 3 mm. aluminum to render the intensity of the Unipuls apparatus as high as possible and yet obtain a radiation possessing a definite hardness.

*Course of the Experiment.*—The test objects were a spawn clump of a pair of rana esculenta. The embryos already had attained form within the membranes. (Fig. 1, table XXI.) The clump was divided into three parts each of 100 animals. One part was radiated with the Unipuls apparatus and the second with the Apex instrumentarium, while the third served as control. The dose in both parts was 125 e. The number of single impulses, within which the doses was applied by the Unipuls machine was 36, the number of interruptions of the Apex machine amounts to 2160 per minute. The total time duration of the radiation with the Unipuls was 193 minutes, that with the Apex 201 minutes. The ratio of intensity can be calculated for both instruments, it is about 1 : 60.

*Extract from the observation journal.*

*Day of radiation:* May 24.

*Days of observation:* June 2. The larvæ have left the membranes and start to swim about. The radiated animals of both groups have shown during the last few days symp-

toms of radiation disease. The radiation symptoms are seen more numerously in the radiated animals of group 1, i.e., about 39 larvæ, than in those of group 2, about 8 larvæ. The symptoms appear to be more distinct in the animals of group 1. (Fig. 2, table XXI.) All the controls are living; one animal each in group 1 as well as in group 2 died.

June 5—An additional 22 animals of group 1 show distinct symptoms of disease and an additional three animals have succumbed. Only one additional animal of group 2 shows symptoms of radiation disease, and an additional two are dead. The controls are all alive.

June 10—All the larvæ of group 1 evidence distinct symptoms of radiation disease; only eight additional animals of group 2 show symptoms. (Fig. 3, table XXI.)

The number of larvæ showing distinct symptoms increased slightly during the continued observations. However, it is shown that the mortality is much greater in the animals of group 1 than in those of group 2. We reproduce a table which shows the number of living animals in each group at the time of the successive observations.

| Day of observation after radiation | Number of living control animals | Number of living animals Unipuls apparatus | Number of living animals Apex Instrumentarium |
|---|---|---|---|
| 7th day | 100 | 100 | 100 |
| 9th " | 100 | 99 | 99 |
| 10th " | 100 | 98 | 99 |
| 12th " | 100 | 96 | 96 |
| 14th " | 100 | 85 | 88 |
| 15th " | 100 | 77 | 88 |
| 17th " | 100 | 68 | 88 |
| 20th " | 100 | 66 | 88 |
| 21st " | 100 | 66 | 83 |
| 26th " | 99 | 49 | 68 |
| 27th " | 99 | 45 | 58 |
| 29th " | 98 | 38 | 53 |

### *Control Experiment.*

*Course of the Experiment.*—The spawn clump of a pair of rana esculenta served as test objects. The embryos had assumed form within the membranes. The clump was divided into three parts, each of 100 animals. Part 1 was radiated with the Unipuls apparatus, part 2 with the Apex instrumentarium, while part 3 served as controls. The dose applied to groups 1 and 2 was 155 e. The number of the impulses of the Unipuls apparatus was 36 per minute, while the interruptions of the Apex instrument were 2160 per minute. The total time duration of application of the radiation with the Unipuls apparatus was 240 minutes, with the Apex instrument 213 minutes. The ratio of intensity may be calculated and is about 1 : 50.

### *Extract from the observation journal.*

*Day of radiation:* May 25.

*Days of observation:* May 30—Eighteen animals of group 1 show distinct symptoms of radiation disease; fifteen animals of group 2 also have symptoms.

*Comparative Observations on the Intensity of the Biologic Action of X-Rays when Applied to the Skin in one Dose or Interval Doses.*

*Course of Observation.*—The latter was made at the time of the radiation treatment of a patient suffering from an inoperable ovarian carcinoma.

The radiation was applied in such a manner that one skin region received one dose of 215 e, while the other homogeneous region received the same dose, but evenly distributed to thirteen sittings on thirteen consecutive days.

*Extract from the observation journal.*

| Field *a*. Radiation with X-rays filtered with 1 mm. copper. Application of 215 e in one sitting. | Field *b*. Radiation with X-rays filtered with 1 mm. copper. Application of 265 e in thirteen sittings, each of 16.5 e. |
|---|---|
| *Day of radiation:* Sept. 25, 1915. | *Days of radiation:* Sept. 27, 1915, to Oct. 11, 1915. |
| Days of observation: | Days of observation: |
| Oct. 14, 1915: Beginning of distinct browning of a small degree. | Oct. 14, 1915: No reaction. |
| Oct. 20, 1915: Distinct erythema of first degree of a reddish color. | Oct. 20, 1915: No reaction. |
| Oct. 26, 1915: Moderately marked erythema of first degree. (Fig. 1, table XXII.) | Oct. 26, 1915: Slight follicular reddening. (Fig. 2, table XXII.) |
| Oct. 30, 1915: Marked reddening with formation of vesicles. | Oct. 30, 1915: Same finding. |
| Nov. 5, 1915: The vesicles begin to raise. More pronounced erythema. (Fig. 3, table XXII.) | Nov. 5, 1915: Almost the same finding. (Fig. 4, table XXII.) |
| Nov. 10, 1915: One-half of the field has peeled; beneath it dry, new skin. | Nov. 10, 1915: Slight reddening, erythema hardly of the first degree. |
| Nov. 17, 1915: Field shows new, regenerated skin. (Fig. 5, table XXII.) | Nov. 17, 1915: Erythema fading. (Fig. 6, table XXII.) |
| Nov. 26, 1915: Normal skin. | Nov. 26, 1915: Normal skin. |

*Control Observation.*

The details were the same as described in the previous experiment.

| *Field a* | *Field b* |
|---|---|
| *Day of radiation:* Sept. 24, 1915. | *Days of radiation:* Sept. 25 to Oct. 9, 1915. |
| *Days of observation:* | *Days of observation:* |
| Oct. 30, 1915: No reaction. | Oct. 30, 1915: No reaction. |
| Nov. 10, 1915: Beginning of mild erythema. (Fig. 1, table XXIII.) | Nov. 10, 1915: No reaction. (Fig. 2, table XXIII.) |
| Nov. 17, 1915: Completely developed erythema of first degree. (Fig. 3, table XXIII.) | Nov. 17, 1915: Very slight, scarcely visible reaction. (Fig. 4, table XXIII.) |
| Nov. 22, 1915: Erythema changed to a blue red with extensive formation of vesicles. | Nov. 22, 1915: Reaction disappeared. Normal skin. |
| Nov. 24, 1915: Erythema begins to fade. The superficial epidermis peels off in dry lamellæ, beneath which new skin is seen. No secretion. | Nov. 24, 1915: Normal skin. |
| Nov. 27, 1915: The desquamation has been completed excepting a few islands; beneath it new skin. (Fig. 5, table XXIII.) | Nov. 27, 1915: Normal skin. (Fig. 6, table XXIII.) |
| Dec. 2, 1915: Normal skin. | Dec. 2, 1915: Normal skin. |

*Result.*

*From these observations we conclude that with like dose and like intensity the degree of the biologic action of X-rays filtered with 1 mm. copper is not the same, if we apply the total dose in one sitting or in daily interval sittings of one-tenth dose. The dose applied in one sitting has a markedly stronger biologic action on the skin surface than the interval dose.*

*Comparative Observations on the Intensity of the Biologic Action of Gamma-Rays of Mesothorium when Applied to the Skin in One Dose and in Multiple Interval Doses.*

*Course of Observation.*—The latter was made on our own skin. Two homogeneous regions of the skin surface were radiated. The radiation was made with a mesothorium preparation of a radioactivity equivalent to 35.5 mg. radium element enclosed in a flat platinum capsule. The capsule was enclosed in a brass-filter of a thickness of 1.5 mm. It rested on a hard rubber ring, which was fixed to a celluloid sheet of a thickness of 2 mm. (See Fig. 61.) The distance of the brass-filter from the skin was 15 mm.

Field *a* was radiated in one sitting of a duration of fifty hours. Field *b* was radiated for five hours on ten consecutive days, i.e., in interval doses.

*Field a.* Time duration of radiation, fifty consecutive hours from 8 P.M., April 8, 1915, to 10 P.M., April 10, 1915.

*Days of observation:*

April 23: Skin reaction not visible.

April 25: In the center of the field a few skin follicles begin to redden.

April 27: The follicle reddening is distinctly marked. (Fig. 1, table XXIV.)

May 2: The follicular reddening in center has become more intensive.

May 9: The central follicular reddening is now confluent.

May 16: In the center of the confluent follicular reddening a small part of the superficial epidermis is raised in the form of a vesicle.

May 19: The central erythema is secreting and covered with a thick scab. (Fig. 3, table XXIV.)

May 23: The scab commences to separate.

May 26: The scab has become separated almost entirely.

May 31: Half of the scab has dropped off. (Fig. 5, table XXIV.)

June 5: Scab fell off.

June 10: Slight radiant scar.

June 20: The soft radiant scar is still visible.

*Field b.* Radiations in sittings of five hours each, from 9 A.M. to 2 P.M. daily from April 11, 1915, to April 20, 1915.

*Days of observation:*

April 23: Skin reaction not visible.

April 25: In the center of the field very slight signs of reddening of hair follicles.

April 27: Follicle reddening scarcely visible. (Fig. 2, table XXIV.)

May 2: The central follicular reddening is more distinctly marked, yet less intensive than in field *a*.

May 9: The central follicular reddening starts to conflux.

May 16: The confluent central follicle formation has increased somewhat in intensity. The superficial layer of the epidermis is not raised and vesicles have not formed.

May 19: Scab formation does not occur because vesicles have not formed. (Fig. 4, table XXIV.)

May 23: The erythema fades without having formed a scab.

May 26: The erythema almost completely gone.

May 31: Erythema healed without formation of scar. (Fig. 6, table XXIV.)

June 20: Normal skin free from scars.

### *Control Observation.*

*Course of the Observation.*—The details correspond in every point to those above described, with the only difference that the celluloid plate of 2 mm. was replaced by one of 5 mm. to assure an arrest of the secondary beta-rays arising in the metal filter.

Field *a* is radiated with the same mesothorium preparation described in the preceding observation for a time duration of fifty hours, from 10 A.M., July 31, 1915, to 12 P.M., August 2, 1915.

Field *b* is radiated five hours each on ten consecutive days, always in the afternoon from August 2, to August 12, 1915, inclusive.

*Field a.* Radiation from 10 A.M., July 31, 1915, to 12 noon, Aug. 2, 1915.

*Days of observation:*

Aug. 14: No reaction.

Aug. 18: Very light, beginning reddening.

Aug. 28: Distinct reddening in the center of the radiation field.

Sept. 2: Pronounced confluent reddening in center of field. The most superficial layer of the epidermis is raised in form of a small blister. (Fig. 1, table XXV.)

Sept. 7: The vesicle has opened in its entire extent.

Sept. 12: In place of the blister a secreting surface.

Sept. 15: Formation of a scab in place of the detached vesicle. (Fig. 3, table XXV.)

Sept. 20: Half of scab has dropped off; progressive healing.

Sept. 25: Scab almost completely detached. A fine, slightly reddened scar corresponding to the place of the detached scab. (Fig. 6, table XXV.)

*Field b.* Radiations afternoons from August 2 to August 12, 1915, inclusive.

*Days of observation:*

Aug. 14: No reaction.

Aug. 18: No reaction.

Aug. 28: No reaction.

Sept. 2: Beginning of a very faint reddening in the center of the radiation field. (Fig. 2, table XXV.)

Sept. 7: Distinct reddening in center

Sept. 12: The most superficial layer of the epidermis has been detached in the form of a blister. Secretion is just beginning.

Sept. 15: Erythema much lighter than in field *a*. Slight secretion, but no formation of scab. (Fig. 4, table XXV.)

Sept. 20: Beginning to heal. A scab has not formed. Secretion disappeared.

Sept. 25: A scar formation did not develop. (Fig. 6, table XXV.)

### *Another Control Observation.*

The details of the observation differ from the previous ones in so far as the intervals of the dose have been extended to twenty-five days.

Field *a* is radiated with the same mesothorium capsule used in the preceding observations in one sitting of fifty hours from 12:30 P.M., August 18, 1915, to 2:30 P.M., August 20, 1915.

Field *b* is radiated daily for two hours on twenty-five successive days, namely, from August 20, 1915, to September 13, 1915, inclusive.

*Field a.* Radiation from 12.30 P.M., Aug. 18, 1915, to 2.30 P.M., Aug. 20, 1915.

*Days of observation:*

Sept. 6: No reaction.

*Field b.* Radiation daily for two hours from Aug. 20 to Sept. 13, 1915, inclusive.

*Days of observation:*

Sept. 7: On account of the frequent removal of the capsule, the skin is irri-

| | |
|---|---|
| Sept. 12: Beginning of distinct reddening in the center of the radiation field. | tated in various places, due to the adhesive plaster. A reddening in the center is clearly visible. |
| Sept. 15: Distinct central reddening. (Fig. 1, table XXVI.) | Sept. 15: Superficial loss of epithelium in the center and brown red discoloration of the extra peripheral space. Probably due to the irritation caused by the frequent removal of the capsule. (Fig. 2, table XXVI.) |
| Sept. 27: Distinct formation of scabs upon a red base. (Fig. 3, table XXVI.) | Sept. 27: Distinct formation of scab in center. (Fig. 4, table XXVI.) |
| Oct. 2: Reddening commences in the surroundings of the scab. | Oct. 2: The scab begins to separate gradually. |
| Oct. 5: The reddening becomes more intensive; the scab also increases visibly in size. | Oct. 5: Half of the scab has dropped off. The epidermis of the surroundings has become detached in large lamellæ. |
| Oct. 8: The scab is the size of a dollar and surrounded by an intensely inflammatory reddening. (Fig. 5, table XXVI.) | Oct. 8: Two-thirds of the scab has dropped off. In the surrounding region normal skin is again seen beneath the epidermis that became detached by the blisters. (Fig. 6, table XXVI.) |
| Oct. 12: Almost the same findings as on Oct. 8. | Oct. 12: Almost the same findings. |
| Oct. 14: The reddening begins to heal; the heavy scab dries up. | Oct. 14: In place of scab a radiant scar appears. |
| Oct. 16: The reddening has completely disappeared, scaling off of the scab. | Oct. 16: Only a small remnant of the scab is seen. |
| Oct. 18: Scab has completely dropped off; large, radiant scar. | Oct. 18: Radiant scar of mean intensity. Scab dropped off. |
| Oct. 20: The same findings. (Fig. 7, table XXVI.) | Oct. 20: Same findings as Oct. 18. (Fig. 8, table XXVI.) |
| Oct. 23: The same findings. | Oct. 23: Same findings. |
| Oct. 30: White, radiant scar. | Oct. 30: White, radiant scar of scarcely half of the intensity as in field *a*. |

*Result.*

*With like dose and like intensity the degree of the biologic action is not the same if the dose is applied in one sitting or in daily interval sittings on 10 respectively on 25 successive days. The single application of the dose has a stronger biologic action on the skin than the interval applications of the same dose.*

*Summarizing the results of all these experiments it has been demonstrated that the intensity of the biologic action is not the same if the dose is applied in one sitting or in divided sittings. The single dose is biologically more intensely active than the interval doses.*

## Biologic Observations on the Influence of Factors Like Diathermy, Heat, Secondary Radiations on the Intensity of the Biologic Action of X- and Gamma-Rays

Attempts have been made to influence the intensity of the biologic action of X-rays by combining the X-rays with other procedures. A comprehensive literature about such combined procedures has been placed before us and we refer amongst others to the monograph

of Müller-Immenstadt who has particularly employed such combined procedures in the treatment of cancer. These high frequency currents have been used to decrease the biologic action of X-rays under certain conditions, for instance to desensitize the skin. Others have used diathermy to increase at selected places of the biologic object the biologic action of rays, for instance to induce an increased action on the carcinoma. Further hot and cold applications have been made use of, respectively chemical means, as adrenalin, have been employed. Finally secondary radiations have been applied as factors to decrease or increase the biologic action.

The clinical proof of the importance of these factors meets with great difficulties, because so many other factors must be reckoned with in such clinical questions, which compel us to be very conservative in our conclusions.

In the experimental biologic tests of these combined procedures, even with more simple conditions of the experiment, difficulties are encountered and we could consider only uncomplicated procedures within the limits of our experimental investigations. We next will attempt to solve by experiment the question: Is the intensity of the biologic action of X-rays influenced by diathermy?

## The Influence of Diathermy and Heat on the Intensity of the Biologic Action of X-Rays

Diathermic currents increase the temperature of the biologic object through which they pass. The stronger the diathermic current the higher the temperature rises in the biologic object with otherwise like conditions.

Two effects may thereby occur in the biologic object: 1. The effect of heat, and 2, the effect of electricity.

Before we begin the investigation of the influence of diathermy we must determine whether a difference in the biologic action exists between the application of ordinary heat and that produced by diathermy. We investigated this problem in frog larvæ and chose the following arrangement of the experiment. The stand for carrying the frog larvæ was placed into the glass bowl G (Fig. 50), so that the larvæ were kept 5 cm. beneath the surface of the water. At two diametrically opposed places of the glass vessel were placed two electrodes E of silver sheeting, 12 cm. long and 8 cm. wide, which served to conduct the diathermic current through the pond water, and therefore also through the frog larvæ. The temperature raised in the water by the diathermy current was determined with the thermometer Th. This arrangement served for the heating of the frog larvæ by diathermy. A second vessel of the same dimensions served for the increase in temperature of the frog larvæ by the application of heat. The arrangement of the experiment was otherwise like the one described previously. Naturally the electrodes of

the diathermic current were absent. To increase the temperature of the water, the glass trough G1 was placed in a larger one G2, in which warm water was kept circulating. The glass trough G2 was surrounded with the heat protector W.

*Course of the Experiment.*—The spawn clump of a pair of rana esculenta served as test object, the larvæ had already assumed form within the membranes. The frog spawn was divided into three parts. The first part was exposed to the diathermic current. The source of the diathermic current was a diathermy apparatus of Siemens and

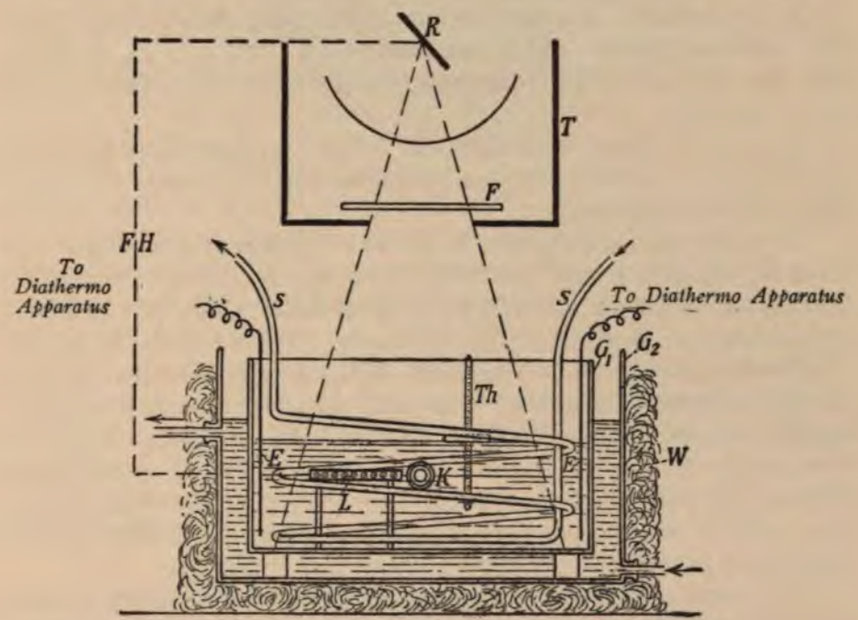



FIG. 50.

Halske, provided with a safety spark gap. The strength of the diathermy current in the glass trough was regulated so that the water increased from the room temperature of 16° C. to that of 30° C., and was kept constant at this point. The current was on an average 0.5 ampère. The second spawn clump was also heated to 30° C., and kept constant at this temperature by water circulating around the glass trough G1. A third spawn clump finally served as a control.

The spawn was kept for three hours at a temperature of 30° C. The time period corresponded to the one required for the application of the X-ray dose.

A series of experiments were made. The results are as follows: An increase of the temperature of the frog larvæ from 16° to 30° C. has no damaging influence on the development of the larvæ, it does not matter whether the increase in temperature was caused by diathermy or ordinary heat. We saw, in conformity with other authors, that the elevation of temperature was followed by a hasten-

ing of the development of the frog spawn during the time of the increase in temperature in comparison to the controls. The larvæ subjected to heat showed during the three hours a veritable advance in development while the controls did not develop any further. The phenomena were the same whether the increase in the temperature of the frog spawn was attained by diathermic currents or by the application of heat.

The diathermic current purely asserts an effect of heat. An electrical effect could not be observed. An increase in temperature to 40° in both groups caused the same mortality in both groups.

In these experiments the strength of the diathermic current which circulated through the water was maintained at 0.5 ampère, as otherwise too high an increase in the temperature of the frog spawn would have occurred.

To find out whether an electrical effect perhaps might be recognized if a much stronger current permeated it, the details of experiment had to be changed.

The resistance of the pond water was so great that stronger currents of the diathermy apparatus could not be passed through it. We, therefore, used an addition of sodium chloride of 1 per thousand to increase the conductivity of the water. Sodium chloride had no visible influence on the development of the frog larvæ. As the temperature of the water would become too high with stronger diathermic currents, it had to be reduced by a proper cooling system. This was obtained by the use of a glass spiral pipe S, placed in the glass trough, through which cold water was kept running. The cooling pipe enabled one to keep the temperature constantly at 30° C. The diathermic current could thus be raised to 1.5 ampère.

The results obtained with this increased current remained exactly the same as in the preceding experiments, i.e., in spite of the increase in the strength of the current, the frog spawn exposed to the higher current did not show any changes in development in comparison with those kept at a temperature of 30° for three hours in the water by the simple application of heat. Here also the effect of heat was solely active in spite of the increase in the diathermic current.

In the experiments just described we observed the effect of diathermy and application of heat on the frog larvæ and saw that they were essentially expressed in a more rapid development of the frog larvæ during the time of increase in temperature. We may now proceed to the investigation of the combined procedures, diathermy and X-rays as well as heat and X-rays.

We carried out the experiments as follows: We compared the intensity of the biologic action of the roentgen dose on frog spawn kept at a room temperature of 16° C., with the intensity of the biologic action of the same roentgen dose on frog spawn, the temperature of which was increased to 30° C. by diathermy, and further with

the intensity of the biologic action of the same roentgen dose on frog spawn the temperature of which was elevated to 30° C. by the application of ordinary heat.

The details of the experiments were as follows:

The glass trough G1, in which the frog spawn was placed 5 cm. beneath the surface of the water, was heated at one time by diathermy and at another by heated water circulating around it. The X-ray tube R was placed above the vessel at a focal distance of 50 cm. The filter consisted of 10 mm. aluminum.

*Course of the Experiment.*—The frog spawn of a pair of rana esculenta served as test object. The larvæ had already assumed form within the membranes. The spawn was divided into three parts, each of 100 larvæ. The first part was exposed at the same time to diathermic currents and X-rays. The intensity of the diathermic current within the glass trough was regulated so that the water was increased from the room temperature of 16° to 30° C., where it remained constant. The current had an average strength of 0.5 ampère. The roentgen dose applied was 125 e. The radiation was begun as soon as the temperature of the water had been raised to 30° C.

The second part of the frog spawn was placed in the same glass trough and in the same place. The temperature of the water was kept at the room temperature of about 16° C. The dose applied was also 125 e with the same filtration and the same duration of radiation.

The third part was kept at a room temperature of 16° C. It was not radiated and served as control.

At the close of the radiation the larvæ were reared in the customary manner.

*Extract from the observation journal.*

*Day of radiation:* May 29, 1916.

*Days of observation:*

June 8—All the larvæ have left the membranes. The radiated animals do not show any distinctly marked symptoms of the radiation disease.

June 14—Of the radiated animals kept at room temperature eleven have died with characteristic symptoms of the radiation sickness. An additional fifty-four larvæ evidence distinct symptoms of the disease.

Of the animals subjected to diathermy and radiation none have succumbed so far, but eighty show distinctly marked symptoms of radiation disease.

Two of the controls have died. The others are all living and of normal development.

June 21—Of the radiated animals kept at room temperature fifty-five are dead. The remaining larvæ show characteristic symptoms of radiation disease.

Of the larvæ subjected to diathermy and radiation, fifty-three have died. The remaining larvæ have characteristic symptoms of radiation disease.

Of the controls an additional three larvæ have succumbed; the others show normal development.

June 26—The radiated animals of groups 1 and 2 are all dead.

Of the controls no additional larvæ have died.

*Result.*

*A difference in the intensity of the biologic action of the same roentgen dose on frog larvæ kept at room temperature and on frog*

*larvæ, the temperature of which has been raised to 30° C. by a diathermy current of 0.5 ampère, is not distinctly recognizable.*

As by the elevation of the temperature a visibly more rapid development of the frog larvæ during the radiation could be recognized, this observation contradicts in a certain sense the customary view that more rapidly growing cells are less resistant to radiations than slowly growing cells.

We have also performed a series of experiments in which the diathermic current was increased to 1.5 ampère, while the temperature of the water was kept at 30° C. by the cooling system.

The course of the experiment closely adhered to the preceding test in every detail; dose and filtration also remained the same.

The result was the same as one would have expected from the preliminary tests. A recognizable influence of diathermy on the intensity of the biologic action of the X-rays was not evident.

We had demonstrated in the preliminary experiments that a diathermic current which increases the temperature of the frog larvæ to a definite degree has no other biologic action than an application of ordinary heat. If we let a known dose of X-rays act on frog spawn kept at the same elevation of temperature by diathermy or ordinary heat, a difference in the biologic action will probably not be seen. Nevertheless it was necessary to confirm this by an experiment.

The details of the experiment were the same as stated in the preceding paragraphs. The temperature of both radiated groups was 30° C., while the controls were kept at the room temperature of 16° C. The radiation of both groups was performed at the same time, the filter was the same and the doses were 125 e.

*Course of the Experiment.*—The spawn clump of a pair of rana esculenta served as test object. The larvæ had assumed form within the membranes. The spawn clump was divided into three parts, each of 100 larvæ. Two groups were radiated, the third group served as control and was kept in the radiation room well protected from the rays.

*Extract from the observation journal.*

*Day of radiation:* May 27.

*Days of observation:*

June 7—Of the animals radiated and subjected to applications of ordinary heat, seventeen died; the others do not show any marked symptoms of radiation disease.

Of the animals radiated and heated by diathermic currents, three have succumbed. The others also do not evidence any marked symptoms of radiation disease.

The controls are all alive and of normal development.

June 10—All the surviving animals radiated and treated with ordinary heat have pronounced symptoms of radiation disease.

The surviving animals of group 2 radiated and exposed to diathermic currents show pronounced symptoms of radiation disease.

Of the controls, one animal died. The others evidence normal development.

June 17—Of the animals of group 1, eighty have succumbed.

Of the animals of group 2, forty-five have died. The survivors show pronounced symptoms of radiation disease.

Of the controls, none have died.

June 19—All the larvæ of groups 1 and 2 have perished with symptoms of radiation disease. The survivors of the controls are all alive and are of normal development.

*Result.—The intensity of the biologic action of X-rays is the same with increased temperature, irrespective of whether the increase in temperature was attained by diathermy or by applications of ordinary heat.*

*Summarizing the results of all these experiments, it has been demonstrated in the frog larvæ as test objects that diathermy and applications of heat have no recognizable influence on the intensity of the biologic action of X-rays.*

The application of the results obtained in the frog larvæ to the human body is not admissible. In the frog larvæ the entire organism is penetrated by the diathermic currents and thus brought to an increased temperature, while the application of diathermy in the human is usually a local one, that is, only part of the organism is permeated and heated by the current. The cold blooded nature of the frog larvæ also plays an essential rôle. The observations on the human therefore do not coincide with the results gained from frog larvæ. In the human, in opposition to the observation in frog larvæ, an influence of diathermy on the intensity of the biologic action of a known dose of X-rays is observed in the sense that the biologic action is generally enhanced by the influence of diathermy. This conclusion conforms to the statements in the literature and is explained by an increased blood supply of the tissues acted upon by diathermic currents. We will desist from an extensive publication of these observations at this time and reserve them for future publication since the experiments have not as yet been concluded.

### *The Importance of Secondary Rays in the Radiation with X-rays or Rays from Radium and Mesothorium.*

If the rays of radium and mesothorium or the X-rays strike upon a body, then the latter gives rise to a new radiation, the secondary radiation. The latter may be a corpuscular radiation and a radiation of the character of wave rays. The rôle which this secondary radiation plays in the principles of radiation therapy, has been already discussed in the first part in reference to purely physical questions.

In this Section we shall discuss the biologic importance of both kinds of these secondary rays. Two groups of observations are necessary. In the first group the secondary radiation arises without the biologic body and acts from without upon the latter. In this case the filter employed must be almost exclusively considered as the secondary radiator. In the second group the secondary radiation is formed within the biologic body itself.

*Biologic Importance of the Secondary Rays arising in the Filter by the Use of Mesothorium and Radium-rays.*

In deep radiation filters are always used which serve the purpose to keep away from the biologic object the beta-rays arising from the radium mesothorium, because these rays have a low penetrability and are absorbed in the most superficial tissue layers, where they would produce an undesirable and strong biologic action. Filters were employed which according to our knowledge of known physical measurements would absorb the primary beta-rays arising in radium and mesothorium. From purely practical considerations, chiefly to prevent the choice of thick filters, one preferred filters of metals of high atomic weight, the so-called heavy metals as lead, gold, nickel and brass.

All these filters, as is known from physical investigations, possess the property when struck by radium or mesothorium rays, to send out secondary beta-rays besides the scattered gamma-rays. The latter are not of any importance in the present controversy as they possess the same characteristics as the primary gamma-rays. The intensity of the secondary beta radiation measured with the ionization method is relatively large compared to the gamma radiation. We have seen in the comparative observations on the biologic action of the beta-rays of uranium-x and the gamma-rays of mesothorium, that with the use of the ionization method as dosation method the beta-rays exercise the same intense biologic action as the gamma-rays. It was, therefore, to be expected that on account of the proportionately great intensity of the secondary beta-rays arising from the filter the beta-rays would partly contribute to the biologic action which must not be neglected.

We have proven the correctness of this assumption in our biologic test object, the frog larvæ. If we filter the rays of radium or mesothorium with 1.5 mm. brass plus 5 mm. celluloid, the brass serves the purpose of arresting the primary beta-rays and the soft gamma-rays. The additional filter of celluloid serves to reduce to a minimum the considerably strong secondary beta-rays arising from the brass filter. Therefore if we let act on the frog larvæ at one time the rays of mesothorium filtered only with brass, and at the other time the rays filtered with brass plus celluloid, both within the same time period, then the biologic action of the secondary beta-rays must be obtained.

*Details of the Experiment.*—The radium cannon served as the radiation apparatus. It was loaded in the usual manner. The cannon was closed on the under surface with a sheet of brass 1.5 mm. thick. The frog spawn was placed in two rectangular glass jars a and b, each had a height of 10 cm., a width of 10 cm., and a length of 16 cm. The spawn was placed on stands so it was just covered with water. (See Fig. 51.) The glass jar b was covered with a celluloid

plate of 5 mm., while the glass jar a was left uncovered. The glass jars were placed close to one another so that the spawn in a and b was radiated at the same time by means of the cannon. The cannon was continuously rotated during the course of the radiation to distribute the radiation evenly to both jars.

*Course of the Experiment.*—The spawn clump of a pair of rana esculenta served as test object. The eggs had so far developed that the embryos had left the membranes and were swimming about in

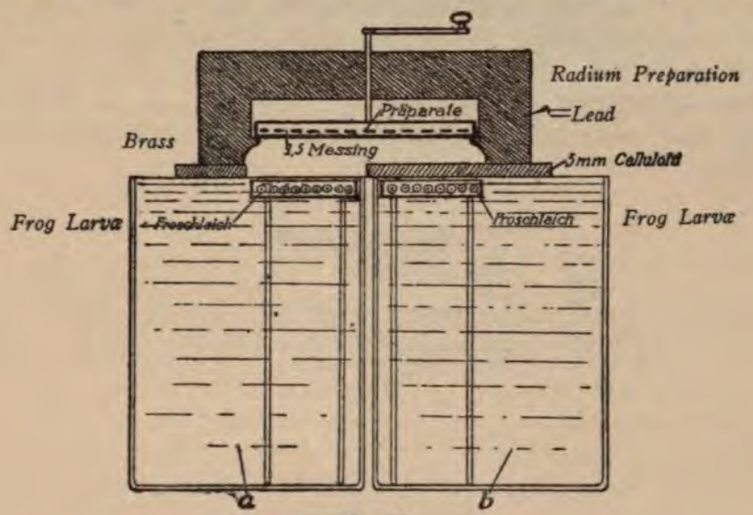



FIG. 51.

the water. The time duration of the radiation was fourteen hours. The dose was 70 e measured with the aluminum chamber dosimeter. The distance of the brass filter from the larvæ was 3 cm. The third part of the frog larvæ, descended from the same family, was kept as a control in a similar glass jar in the same location and under the same external conditions.

### *Extract from the observation journal.*

*Day of radiation:* June 5.
Jar *a* without celluloid filter.
*Days of observation:*
June 7—The larvæ show the vesicular swellings of radium sickness.

June 8—All the animals are dead, with the characteristic symptoms of the radium disease.

*Day of radiation:* June 5.
Jar *b* with 5 mm. celluloid filter.
*Days of observation:*
June 7—The larvæ show distinct symptoms of radium disease but are more lively and mobile than the larvæ in jar *a*.
June 8—The animals are living; the vesicular swellings are more pronounced.

June 10—A small number of the larvæ have died. The survivors are backward in growth in comparison to the controls.
June 12—Only a small number are still living. The survivors show a marked retardation in growth in comparison to the controls.
June 18—All the animals have died. Also a few of the controls.

*Result.*

This experiment shows that the secondary beta-rays, arising from the brass filter during the radiation with radium and mesothorium, have an important place in the biologic action.

The observation has clinical importance because in deep radiation we must radiate through the skin, and the share which the secondary beta-rays have in the biologic action will be chiefly absorbed in the upper layers of the skin on account of the low penetrability of the secondary rays. We, therefore, performed analogous observations on our skin.

The details of the experiment conformed closely to those used in the frog larvæ. We could not use the large amount of radium

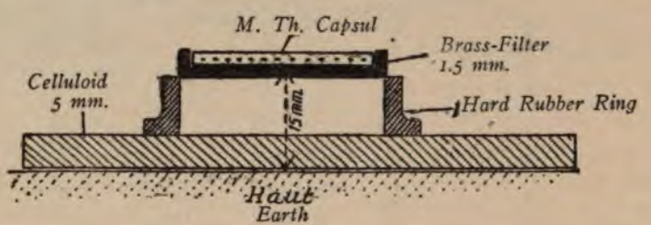



FIG. 52.

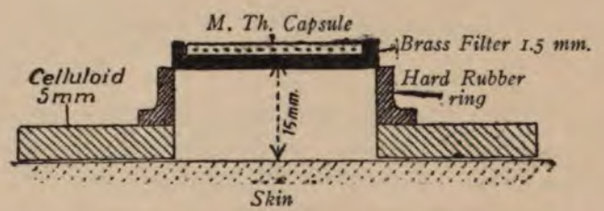



FIG. 53.

and mesothorium as in the frog larvæ, as we would have obtained an erythema of too great an extent. We used a flat mesothorium capsule of a diameter of 27 mm. and a thickness of 4 mm., with a gamma-ray radiation of 37.8 mg. radium element.

Two homogeneous regions of the skin were radiated. The skin field *a* was radiated as shown in Fig. 52. The mesothorium capsule was mounted on a hard rubber ring which was placed on a celluloid plate 5 mm. thick. The latter extended 2 cm. all around beyond the hard rubber ring. In the radiation of the skin region *b* the mesothorium capsule was placed on a hard rubber ring without celluloid plate, as seen in Fig. 53. In skin field *a* the secondary beta-rays, arising from the brass filter, were arrested by the additional celluloid filter, while in field *b* the secondary beta-rays acted upon the skin. The time-duration of the radiation was twenty-five hours for field *a* as well as for field *b*.

*Extract from the observation journal.*

| Field *a* | Field *b* |
|---|---|
| *Radiation:* Oct. 15, 1915, at 12 noon, 25 hours with mesothorium capsule equivalent to a radium element activity of 38.7 mg. The skin was protected from the secondary beta-rays by 5 mm. celluloid. | *Radiation:* Oct. 17, 1915, at 8.30 A.M., 25 hours with mesothorium capsule equivalent to a gamma-ray activity of 38.7 mg. radium element. The skin was not protected from the secondary beta-rays. |
| *Days of observation:* | *Days of observation:* |
| Oct. 30: No reaction. | Oct. 30: No reaction. |
| Nov. 8: No reaction. | Nov. 8: Beginning of light follicular reddening. |
| Nov. 13: Very light beginning follicular reddening. | Nov. 13: The reddening has become more distinct. |
| Nov. 17: Same findings. | Nov. 17: Light, confluent erythema. |
| Nov. 19: Light, confluent erythema. | Nov. 19: The erythema assumes a darker shade and shows small vesicles at the hair follicles. |
| Nov. 22: Same findings. | Nov. 22: A blister forms on a bluish red base. |
| Nov. 25: Same findings. | Nov. 25: The vesicle has ruptured and shows a secreting base. |
| Dec. 20: The erythema has disappeared and did not progress beyond the follicular reddening. | Dec. 20: The erythema has partly healed with the formation of a scab, which is still visible at a small place. |

*Result.*

*This experiment shows the pronounced share of the secondary beta-rays in the biologic action.*

To obtain somewhat of a quantitative presentation of the biologic action of the secondary beta-rays we add an absorption graph of

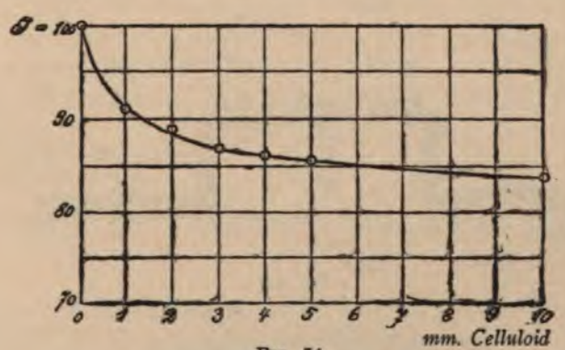



FIG. 54.

the rays passing through the 1.5 mm. brass filter from the mesothorium capsule used in the last experiments, which was obtained by the measuring method described on page 10 of the physical part. See Fig. 54.

The thickness of the radiated celluloid layer is entered in millimeters on the abscissa, while the intensity of the ionization is entered on the ordinate expressed in the percentage of the surface intensity. We see from the course of the graph that a considerable

beta radiation is present which, however, has become practically absorbed after passing through 5 mm. celluloid. If we regard the amount of the ionization as a measure of intensity, then it follows from the graph that the beta radiation arising in the brass filter amounts to about 15 per cent of the total radiation.

As pronounced as the biologic action of these secondary beta-rays appears to be, we must not forget that the action of the secondary beta-rays, analogous to the experiments with uranium-X, is confined to the upper layers of the skin on account of their low penetrability. It is clinically of sufficient importance because the intensity of the biologic action of these secondary beta-rays (if they are not arrested) on the skin may be undesirably severe, without a corresponding increase of the intensity of the biologic action in the depth.

*The Dependence of the Intensity of the Biologic Action of Secondary Beta-Rays that arise on the Filter of Various Materials with the Same Gamma Radiation.*

The intensity of the secondary beta-rays is dependable on the filter material. It is the greater, the higher the atomic weight of

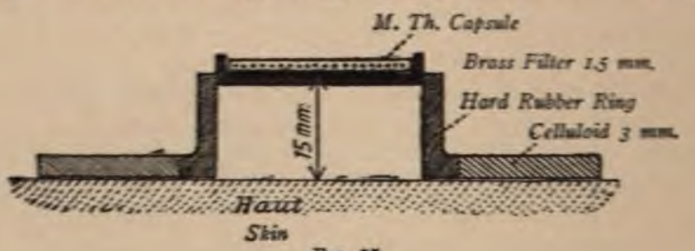



FIG. 55.

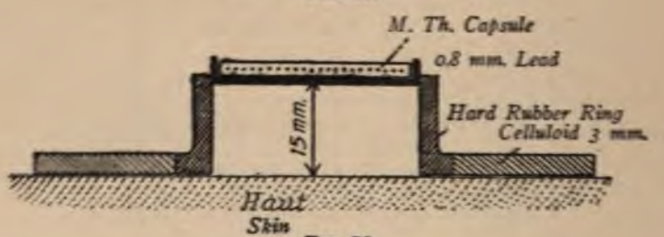



FIG. 56.

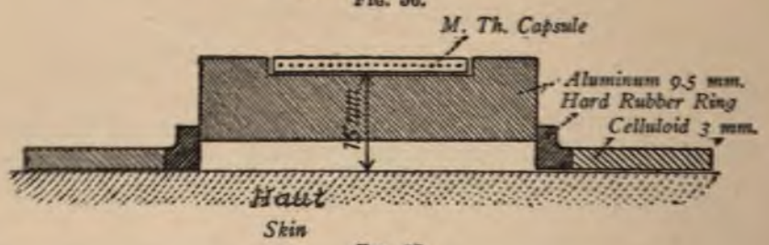



FIG. 57.

the filter is. The biologic action will vary in intensity depending on the kind of filter material employed. The difference in the in-

tensity of the biologic action is best represented, if the thicknesses of the various filters are selected so that the primary beta-rays will become absorbed and that the gamma-rays remaining are of an equal intensity after penetrating the various filters.

We found in our physical investigations of the secondary beta radiation, that the gamma radiation of a mesothorium capsule of a diameter of 27 mm. and a thickness of 4 mm. was then the same if the thickness of the filter was 9.5 mm. for aluminum, 1.5 mm. for brass and 0.8 mm. for lead. With these thicknesses of filter the primary beta radiation was practically absorbed. The secondary beta radiation arising from these filters expressed in per cent of the gamma radiation was 13 per cent with aluminum, 15 per cent with brass, and 20 per cent with lead.

The mesothorium capsule had a gamma-ray activity equal to 38.7 mg. radium element. It was mounted on a hard rubber ring so that the distance of the capsule from the skin was 15 mm. See Figs. 55, 56 and 57.

The capsule is filtered laterally and beneath by 9.5 mm. aluminum in the experiment a, by 1.5 mm. brass in experiment b, and by 0.8 mm. lead in experiment c.

To confine the action to a certain region of the skin, the hard rubber ring is placed on a celluloid plate 3 mm. thick, which arrests the secondary beta rays. This plate extends for 2 cm. all around beyond the rubber ring, while the space within the ring was left open.

The time duration of the application was forty-five hours for each of the experiments.

| a. Use of an aluminum filter 9.5 mm. thick. | b. Use of a brass filter 1.5 mm. thick. | c. Use of lead filter 0.8 mm. thick. |
|---|---|---|
| *Radiation:* 6 P.M., April 5, 1915, left infra-clavicular region, 45 hours to 3 P.M., April 7. | *Radiation:* 8 P.M., April 1, 1915, right infra-clavicular region, 45 hours to 5 P.M., April 3. | *Radiation:* 9 P.M., April 3, 1915, region above xyphoid process, 45 hours to 6 P.M., April 5. |
| *Days of observation:* | *Days of observation:* | *Days of observation:* |
| | April 5: Beginning of reddening in center of field. | April 5: Beginning of reddening in center of field. |
| | | April 6: Central reddening distinct and stronger than in Fig. 2, table XXVII. |
| April 9: First appearance of a slight reddening in center of field. (Fig. 1, table XXVII.) | April 9: Reddening in center has progressed some, but it is just observable. (Fig. 2, table XXVII.) | April 9: Findings as on April 8. Distinct central reddening. (Fig. 3, table XXVII.) |
| April 12: The reddening in center, just visible, has not become stronger. | | |
| | April 19: Findings as on April 9. | |
| April 24: The central reddening grows more distinct. | April 24: The erythema has grown more distinct and larger. Evidences of blistering appear in center. | April 24: The epidermis becomes detached in center due to formation of a blister. |

| | | |
|---|---|---|
| April 27: The reddening is more marked, but of a light degree. (Fig. 4, table XXVII.) | April 27: A vesicle is plainly visible, but not as distinct as in experiment c. (Fig. 5, table XXVII.) | April 27: The blister in center of field is pronounced and secretes some. In the upper half a slight reddening begins to appear beneath the area covered with the celluloid ring. (Fig. 6, table XXVII.) |
| | May 2: The slightly secreting erythema is slowly drying up. A very light reddening is visible at the region of the skin beneath the celluloid ring. | May 2: A scab has formed in place of the secreting erythema. The reddening has very much decreased. May 5: Scab has separated. A secreting area visible beneath it. |
| May 19: The skin has peeled; in center, small scar with slight mottling. (Fig. 7, table XXVII.) | May 19: The blister has become detached. A small, very fine scar with mottling seen in center. Observation closed. (Fig. 8, table XXVII.) | May 19: After partial detachment of the superficial dried layer a radiant, light red colored scar is visible in center. (Fig. 9, table XXVII.) |
| June 15: Barely visible superficial scar. Observation closed. | | June 15: Scar still visible. Essentially more intense than that of a and b. |

### *Result.*

*From the three observations it follows that with the same gamma radiation the intensity of the biologic action is dependable on the filter material.*

The great importance of the secondary beta radiation for deep therapy with radium and mesothorium made it appear desirable to get rid of these radiations if possible. We found that the secondary beta radiation is the weaker, the lower the atomic weight of the filter material. It appears that a filter of low atomic weight, for instance, celluloid, is preferable to a metal filter. In deep therapy the beta-rays and soft gamma-rays must be arrested. Therefore the use of a metal filter of a definite thickness is necessary. To reduce to a minimum the secondary beta radiation arising in this metal filter we saw that 5 mm. celluloid as additional filter was sufficient.

If through the additional filter of celluloid the secondary beta-rays arising from the aluminum, brass or lead filter become arrested through the influence of the filter material, then the biologic action should no longer be recognizable. A second series of experiments should demonstrate this.

*The details of the Experiment.*—The details differ from the preceding experiment in that the hard rubber ring was placed on a 5 mm. celluloid, is preferable to a metal filter. In deep therapy the beta-distance from capsule to skin the hard rubber ring had to be cut down in height. The thicknesses of the metal filters remained the same.

See Figs. 58, 59 and 60. The time exposure for the three experiments was fifty hours in each series.

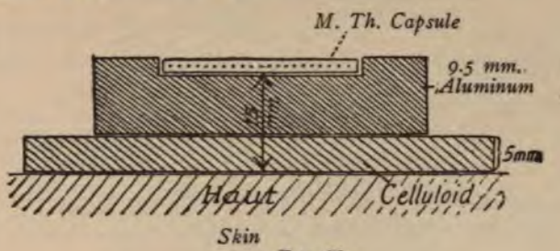



FIG. 58.

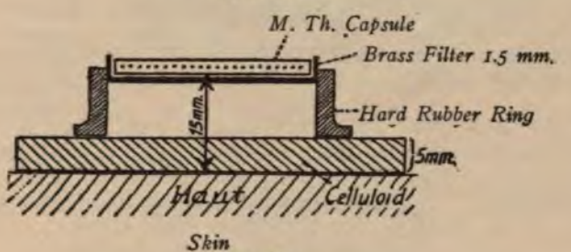



FIG. 59.

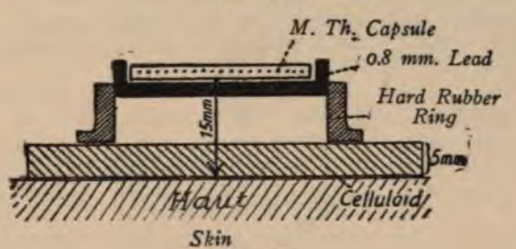



FIG. 60.

a. *Aluminum filter* 9.5 mm. plus celluloid filter 5 mm.

*Radiation:* 7 P.M., May 13, 1915, to 9 P.M., May 15, to skin of left thigh.

*Days of observation:*

May 19: No reaction. (Fig. 1, table XXVIII.)

May 31: No reaction.

June 2: Beginning of very faint follicular reddening within the hard rubber ring. (Fig. 4, table XXVIII.)

b. *Brass filter* of 1.5 mm. plus celluloid filter of 5 mm.

*Radiation:* 7 P.M., May 7, 1915, to 9 P.M., May 9, on enziform process.

*Days of observation:*

May 16: No reaction. (Fig. 2, table XXVIII.)

May 23: Beginning of faint reddening of skin area within the hard rubber ring.

May 26: The central reddening of skin area has grown more distinct.

May 31: Reddening of skin has increased.

June 2: Distinctly marked light follicular reddening within area of hard rubber ring. No reaction external to the hard rubber ring. (Fig. 5, table XXVIII.)

c. *Lead filter* of 0.8 mm. plus celluloid filter of 5 mm.

*Radiation:* 9 P.M., May 10, 1915, to 11 P.M., May 12, to skin of right thigh.

*Days of observation:*

May 16: No reaction. (Fig. 3, table XXVIII.)

May 31: No reaction.

June 2: Beginning of very faint reddening of the skin area within the hard rubber ring. (Fig. 6, table XXVIII.)

| | | |
|---|---|---|
| June 6: The follicle reddening has visibly increased. | June 6: The follicle reddening has become confluent as a diffuse central reddening. | |
| June 9: Beginning confluence of the follicle reddening. | | June 9: The follicles are colored a distinct red. |
| June 11: Diffuse central reddening. | June 11: The superficial layers of skin are slightly detached. Some secretion in center. | June 11: The follicular reddening is becoming confluent. |
| June 16: Beginning formation of small blisters in area of reddening. | June 16: Secretion is drying up with formation of scab in center of field. | June 16: The reddening is now intense and confluent. |
| June 20: The small vesicles are still separated from each other. No reaction external to hard rubber ring. | June 20: The dried central scab begins to desquamate. | June 20: Beginning of formation of vesicle in center with a red base. No reaction external to hard rubber ring. |
| June 23: Two small vesicles have ruptured and form small scabs. (Fig. 7, table XXVIII.) | June 23: The scaling of superficial layers of skin is completed; the base red; apparently no tendency to scar formation. (Fig. 8, table XXVIII.) | June 23: Blister still present and has not yet ruptured. (Fig. 9, table XXVIII.) |
| June 30: Scab grown wider. Vesicles surrounding it have formed folds. (Fig. 10, table XXVIII.) | June 30: Process retrogressing. Epidermis less red. (Fig. 11, table XXVIII.) | June 30: Blister is detached, base secreting; formation of dark brown scab. (Fig. 12, table XXVIII.) |
| July 10: The superficial layers of epidermis detached in folds. A very tender scar. (Fig. 13, table XXVIII.) | July 10: Hardly visible scar; reddening almost completely gone; desquamation of superficial layer of skin at periphery almost completed. (Fig. 14, table XXVIII.) | July 10: The upper layer of epidermis, detached by blisters, has fallen off; also the scab. The base is colored white. A very slight scar visible in place of scab. (Fig. 15, table XXVIII.) |

### *Result.*

*The intensity of the biologic action of mesothorium-rays on the skin after passing filters of various materials—aluminum, brass, lead is different with the total gamma radiation when the secondary beta-rays are not arrested. The strongest biologic action results from the lead filter, the weakest from the aluminum filter.*

*If the secondary beta radiation is arrested by a celluloid filter 5 mm. thick, the intensity of the biologic action of mesothorium-rays on the skin after passing through filters of various materials—aluminum, brass, lead—is with the same total gamma radiation the same.*

*No importance is to be attributed to the filter material, provided that the secondary beta-rays arising in the filter are arrested by an additional filter of celluloid. The brass filter, so often recommended, does not merit any advantage contrasted with lead and aluminum filters*

*Comparative Observations on the Intensity of the Biologic Action of the Secondary Beta-Rays arising from the Brass Filter with Mesothorium and Radium.*

We have exclusively used so far a mesothorium capsule in the experiments on the skin to investigate the secondary beta radiation arising in the filter. A test was deemed necessary to determine whether the secondary beta radiation arising from radium differs from the secondary beta radiation of mesothorium, provided that both radiation preparations have the same gamma-ray activity.

The details of the experiment corresponded to those described on page 152. Between skin and brass filter a celluloid plate of 1/10 mm. thickness was interposed which served the purpose of preventing the bulging of the skin into the celluloid frame. The secondary beta-rays could penetrate the skin unhindered by such a thin sheet of

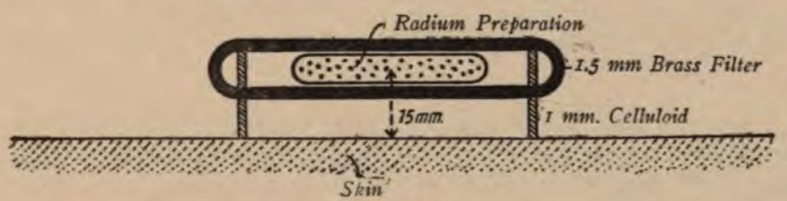



FIG. 61.

celluloid. Fig. 61 presents the arrangement in natural size. The 1/10 mm. celluloid plate has been intentionally omitted in the drawing. The radium and mesothorium preparations mentioned on page 153 were used, as they possessed almost the same radio-activity of 48 mg. radium element. The distance of the mesothorium and radium from the skin was 15 mm. in both radiation frames. Differences in the biologic action must be observable in case the beta radiation arising from the brass filter with radium would vary from that with mesothorium as the same distance, same filtration, same time duration of application of radiation and therefore also the same dose were used.

*Extract from the observation journal.*

Both frames, radium respectively mesothorium capsules, are applied at the same time to homogeneous regions of the outer third of the right and left infraclavicular regions. The time duration of radiation was forty-five hours from 9 P.M., March 22, to 6 P.M., March 24.

| *Days of observation:* a = radium. | |
|---|---|
| March 25: | No reaction. |
| March 28: | No reaction. |
| March 28: | Erythema just beginning. |
| March 30: | Very faint erythema. |

| *Days of observation:* b = mesothorium. | |
|---|---|
| March 25: | No reaction. |
| March 28: | No reaction. |
| March 29: | Just beginning erythema. |
| March 30: | Erythema somewhat more distinct than in field a. |

| | |
|---|---|
| April 1: Slight erythema. (Fig. 1, table XXIX.) | April 1: Distinctly marked erythema. (Fig. 2, table XXIX.) |
| April 4: Erythema somewhat more distinct. | April 4: Erythema extends farther. The bright red color has assumed a more brownish tint. |
| April 8: Brownish mottled erythema. (Fig. 3, table XXIX.) | April 8: Erythema more marked than in field a; in the center a small blister. (Fig. 4, table XXIX.) |
| April 10: Erythema desquamating in fine scales. | April 10: Erythema markedly more intensive than in field a. Erythema desquamating in large lamellæ. |
| April 16: Upper layer of epidermis has been detached by small blisters with beginning secretion of the base. | April 16: Upper layer of epidermis has been removed; base secretes freely. |

April 19—Fields *a* and *b* present almost the same condition. Both fields secrete evenly within the same extent.

April 24—No difference observable in the intensity of the erythema of both fields.

April 27—The erythemata of both fields are healing. (Figs. 5 and 6, table XXIX.)

May 2—Fields *a* and *b* are covered with dry scabs.

May 7—The scabs have fallen off from both fields.

May 28—Both fields show superficial white scars of about the same size. (Figs. 7 and 8, table XXIX.)

June 24—Same findings as on May 28.

### *Result.*

***If we let a radium and a mesothorium capsule of the same gamma-ray activity act on homogeneous regions of the skin after passing a brass filter, under otherwise like conditions, without arresting the secondary beta-rays arising from the brass filter, a distinct difference in the intensity of the biologic action between radium and mesothorium cannot be determined. Though the symptoms appeared somewhat earlier with the mesothorium capsule, the reaction is completely equalized if the observation is continued.***

### *Biologic Importance of the Secondary Radiation arising from the Filter when using X-Rays.*

The corpuscular secondary radiation, which arises from the penetration of a metal filter with X-rays, has a small penetrability in contrast to the secondary beta radiation which arises from the use of gamma-rays. Their extent in air is so small that the radiation scarcely even reaches the biologic object due to the greatest distance from the biologic object usually maintained. If the filter were to be placed on the biologic object, the corpuscular radiation would penetrate into the object, but the extent into the depths would be so small (it amounts to only a fraction of a millimeter) that a biologic action cannot be produced on the biologic object as skin, frog larvæ, etc.

The scattered radiation arising from the filter, which on account of its origin possesses the same composition in regard to hardness as the primary radiation producing it, has an influence on the biologic object according as it influences the quotient of the dose. The scattered radiation tends to let the decrease of the intensity of the radiation arising from the anticathode appear smaller than it would be without filter.

The homogeneous secondary radiation of the filter exerted by the primary radiation might be of greater importance, for it would influence the composition of the radiation striking the biologic object and produce a change in the quotient of the dose due to the low penetrability and thereby an undesirable strong biologic action on the surface of the biologic object. In the literature on deep therapy this secondary radiation of the filter is often referred to as a dangerous filter radiation and an especially destructive action has been ascribed to it. The experiments which have been reported as a proof of this contention, and which are only a repetition of Barkla's investigations, are, according to our opinion, not of a sufficient soundness to prove the great importance of the dangerous filter radiation. Grossmann from theoretical reasoning already pointed to it that with the use of filter material and filter thickness customary in deep therapy, the rays experience such a hardening in the upper strata of the filter that the range of hardness within the dangerous radiation could be excited is not present any more in the rays reaching the most upper strata of the filter. The dangerous filter radiation might be observable on the surface side of the filter facing the X-ray tube, but it is not observable on that side of the filter turned toward the biologic object.

We understand by the customary filter material aluminum, zinc, copper, brass and silver. If filter of highest atomic weight as gold, silver, platinum and tungsten are used, then the formation of the K-series of their own characteristic radiations of these metals by the hard rays employed in deep therapy could cause a dangerous filter radiation. However, such metals have so far not been employed in practice as filters. Investigations on this point are going on and will be published later.

To confirm these suppositions by experiments, a series of investigations was undertaken in which it was demonstrated that as a matter of fact with the use of zinc and copper, the homogeneous secondary radiation of copper and zinc could be observed on the side turned towards the tube and not on the opposite side, if the thickness of the filter was one-tenth of a millimeter. Though the physical proof alone should be sufficient to expel the ghost of the dangerous filter radiation we performed a few biologic experiments and used as test objects the frog spawn.

The course of the experiment was as follows: In the large glass jar a plate P, impermeable to X-rays, was placed 7 cm. above the bottom of the jar. Two squares of a size of 8 by 8 cm. were cut out of the plate, the inner sides of which were parallel to each other and 2 cm. distant from each other. One square (see Fig. 62) was closed on its lower side by a copper filter (Cu.) of a thickness of 0.15 mm., the other square with an aluminum plate (Al) of a thickness of 4 mm. Both filters were placed directly on the surface of the water but so that they would not touch it. The frog spawn was placed in the frame

close beneath the surface of the pond water. The X-ray tube was placed above the center between the squares at a distance of 40 cm. The measuring chamber K of the dosimeter was located beneath the aluminum filter at the same height as the frog spawn.

The thickness 0.15 mm. of the copper filter was so measured that with a certain hardness of the tube which excited the characteristic radiation of the copper according to our physical investigations, the dose measured beneath the copper filter was equal to the one measured underneath the 4 mm. aluminum filter. During the ex-

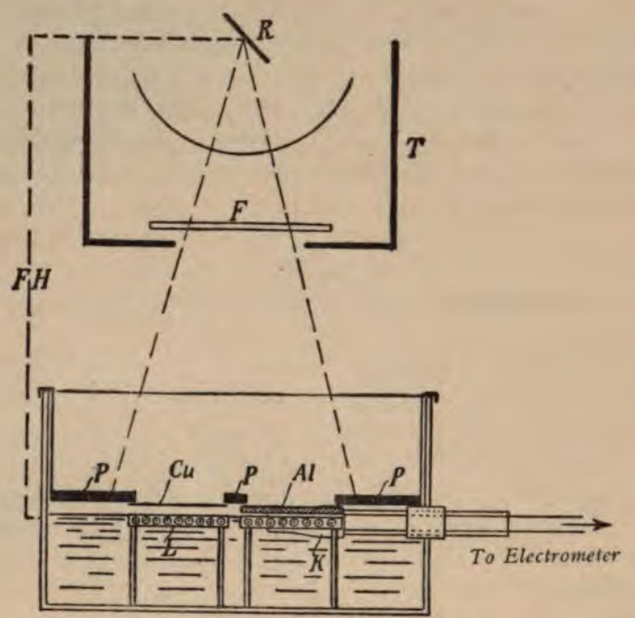



FIG. 62.

periment the hardness of the tube was intentionally varied. On account of these fluctuations in the hardness, the characteristic radiation is excited in varying degrees and corresponding to them the dose, measured beneath the aluminum filter. If a biologic importance could be attributed to the dangerous filter radiation, it would show itself in this experiment on account of the sensitiveness of the frog larvæ.

*Course of the Experiment.*—The spawn of a pair of rana esculenta served for the radiation. It was in the stage in which the embryos just begin to move about. The spawn clump was divided into three parts. Two groups were radiated within the same time. In group 1, the X-rays penetrated the 0.15 mm. copper filter, in group 2, the 4 mm. aluminum filter. Group 3 served as control. A dose of 140 e measured beneath the aluminum filter was applied. The hardness of the tube was continuously changed during the entire duration of the radiation.

*Day of radiation:* June 4.

*Days of observation:*

June 7—Both groups already show marked symptoms of the radiation sickness; both groups show the signs of abdominal dropsy at about the same time and of the same degree.

June 10—All the animals of both radiated groups have died and are putrefying.

*Result.*

*This experiment shows that a dangerous filter radiation does not arise in copper of the thickness indicated as filter material.*

*The Biologic Importance of the Homogeneous Secondary Radiation which arises from a Secondary Radiator located externally to the Biologic Object.*

In the experiments made hitherto the secondary radiation was combined with the primary radiation penetrating the filter. A combination of both radiations was therefore tested in their biologic action. It was, however, important to know whether the secondary radiation alone could exercise a biologic action within a time duration of radiation that was practicable. This question has been repeatedly

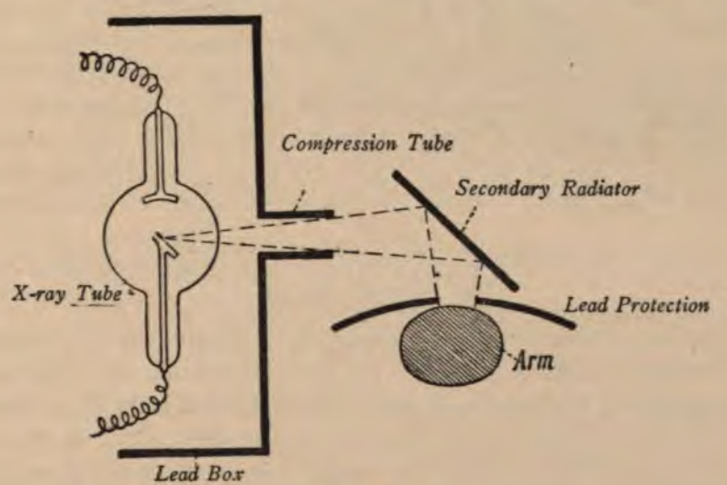



FIG. 63.

discussed in the literature and it appeared to have a certain significance, as one would expect that the homogeneous secondary radiation from bodies of higher atomic weight could give special information about the dependence of the biologic reaction on the hardness of the rays.

The smaller intensity of the fluorescent radiation even in its strongest excitation in comparison to the intensity of the primary radiation led to the expectation that the fluorescent radiation alone would not cause a distinct biologic reaction within the necessary time duration of a radiation. Still we deemed it necessary to confirm this by a few biologic experiments.

We used for these experiments a similar arrangement as was used in the study of the physical properties of secondary radiations and employed as biologic test object the skin. (See Fig. 63.)

From the X-rays arising from the anticathode of a roentgen-tube a beam of a diameter of about 5 cm. was cut out by a diaphragm. This X-ray beam was projected onto a metal plate placed at an angle of 45° to the axis of the beam. The metal plate served as the secondary radiator. Beneath this metal plate the arm was placed at as close a distance as possible, without it being struck by primary rays. The arm was also protected from the primary rays arising from the tube by a heavy lead box which surrounded the tube. A field of 6 sq. cm. was defined by leaded rubber on the forearm and exposed to the secondary radiator. The material of the latter consisted of either a heavy aluminum plate, an iron plate, a zinc plate, or a lead plate.

The Coolidge tube always had the hardness which excited strongly the characteristic radiation of the metals used as secondary radiators. This had been determined by preliminary tests.

The radiation was performed for twelve hours each on three consecutive days. Within these 36 hours from 25 to 30 e were measured on the skin obtained from the secondary rays of the metal plates with the higher atomic weights. The dose was much less with the aluminum plate. A visible irritation of the skin did not appear in any of the tests which coincided with the small dose. The extension of the experiment to a longer time duration of radiation did not appear to be necessary considering the negative value of the question.

### *The Biologic Importance of the Secondary Radiation arising within the Biologic Object.*

Secondary radiations form within the biologic object as they do in all bodies struck by X-rays. We have discussed the influence of these secondary rays on the dose, on the distribution of the radiation in the biologic object, on the quotient of the dose, etc. In these instances the secondary radiation appeared to be of great importance. Above all it contributed to the improvement of the quotient of the dose between the surface and depth of the biologic object. This improvement of the dose quotient permitted the attainment of a relatively intense biologic action in the depth of the biologic object with a relatively small demand on the surface.

If we intend to influence by radiations deep-seated tissues and organs, it is a matter of moment that the tissues lying above it be damaged as little as possible and that the quotient of the dose be as large as possible. Consequently we have attempted to increase the quotient of the dose by introducing a secondary radiator in the biologic object at a place where it was intended to act on an organ or tumor. The secondary radiator should increase the dose by its own radiation at the desired place in the biologic object. It was, for

instance, recommended in the treatment of carcinoma of the stomach with rays to introduce a bismuth meal into the organ. Further, it was proposed to insert metal bougies into the uterus during the radiation for corpus carcinoma, or to inject potassium iodid solutions or collargol into the growth, etc.

The results so far published have not been very encouraging. Comparative investigations with and without secondary radiators also have not been reported. We therefore cannot as yet interpret the favorable action of the secondary radiators.

In order to obtain an idea of the relative importance of such secondary radiations deposited within the tissues, we performed a few physical tests bearing upon this point. These tests had the following results:

If we placed a secondary radiator such as a plate, a metal or a colloidal solution in the water phantom, then the dose was increased just above the secondary radiator, that is, by its own rays between the anticathode and secondary radiator. The dose beneath the secondary radiator was decreased. The strong absorption of the primary radiation in the secondary radiator completely neutralized the favorable action of the secondary radiator. The experiments, which are to be closed in the near future, will be communicated later.

These physical investigations led to the expectation that a relatively small importance should be attributed to the use of secondary radiators in the tissues of the biologic object. In spite of this we have attempted to form an opinion about this matter through biologic experiments. We employed as biologic objects frog spawn and human skin. With the spawn we could best determine the activity of solid secondary radiators; on the human skin best the action of secondary radiators minutely dispersed in the biologic object by using aqueous or colloidal solutions.

### *Experiments on the Biologic Importance of a Sheet of Silver as Secondary Radiator on Frog Spawn*

*Details of the Experiment.*—We used the radiation vessel seen in Fig. 42, in which two rectangular frames were placed close to each other. One of the stands was covered with two layers of gauze, between which the frog spawn was arranged in a single layer. The other stand was covered with a sheet of silver ½ mm. thick, surrounded with a very thin layer of Para rubber. The frog larvæ were placed upon the silver sheet in one layer. The surface of the water just covered the frog spawn in both frames.

The X-ray tube was placed exactly in the center of both frames at a focal distance of 40 cm. In one series of experiments the filter consisted of 3 mm. aluminum, in the other of 1 mm. copper. The ionization chamber of the dosimeter was placed between the stands at the same height as the frog spawn.

*Course of the Experiment.*—The frog larvæ of a pair of rana esculenta served as observation material. The larvæ had just assumed form within the membranes. The spawn clump was divided into three parts, each of one hundred larvæ. Groups 1 and 2 were rayed, group 3 served as control. The dose was 125 e.

*Extract from the observation journal.*

Filtration with 1 mm. copper; dose, 125 e.

*Day of radiation:* April 1, 1916.

*Days of observation:*

April 4—The controls have left the membranes and swim about in the pond water. The larvæ radiated with and without secondary radiator evince the distinct symptoms of the radiation disease in the same degree and have remained behind in development in contrast to the controls.

April 8—The symptoms have progressed in both radiated groups, without any difference being observed between the larvæ of the groups. The animals radiated with the secondary radiator evince rather weaker symptoms.

April 10—The controls are all alive and of normal development.

About the same number in each of the radiated groups have died. The survivors show a progress in the radiation symptoms, without any marked difference between the groups.

April 12—The larger number of animals of the radiated groups have died.

April 16—The controls are developing normally. The animals radiated without secondary radiator are all dead. A few are still living in the group rayed with the secondary radiator, but they succumbed in the next few days.

*Result.*

*The employment of a solid secondary radiator in form of a silver sheet with X-rays filtered with 1 mm. copper does not possess an influence on the intensity of the biologic action on frog larvæ which were placed close above the secondary radiator.*

As the filtration with 1 mm. copper produces rays of great hardness which perhaps but slightly excite the characteristic radiation of silver, we performed experiments with the softer radiations employed by us in deep therapy, namely, X-rays filtered with 3 mm. aluminum, to determine whether silver as secondary radiator assumes some importance with this filtration. We made no experiments with unfiltered or weakly filtered rays which practically do not come into consideration.

Details and course of the experiment remained the same. Only 3 mm. aluminum instead of the 1 mm. copper was selected as filter. The spark-gap applied to the Coolidge tube was the same as already determined in our earlier investigations. The spawn clump of a pair of rana temporaria served as the biologic object. The embryos had just assumed form within the membranes.

*Extract from the observation journal.*

Filtration with 3 mm. aluminum; dose, 125 e.

*Day of radiation:* April 2.

*Days of observation:*

April 7—The controls have left the membranes and swim about in the pond water. The radiated larvæ of both groups show marked symptoms of radiation disease. Difference between the groups cannot be recognized.

April 10—The controls have continued to develop normally. The radiation symptoms in the radiated animals are more pronounced. The animals rayed with the secondary radiator perhaps evince the symptoms in a somewhat larger number of larvæ.

April 16—The controls are in normal development. The slight difference in the number of symptoms between the radiated groups has become equalized in the meantime. A difference cannot be seen. Some of the animals of both groups have succumbed.

April 20—The controls are in normal development. A large number of the animals of both radiated groups has succumbed. The animals rayed without the secondary radiator again evince stronger symptoms and have remained behind in development more than the others.

April 22—All the radiated animals are dead, while the controls are in normal development.

Several control experiments show the same results.

From the experiment it is seen that, similar to the filtration with 1 mm. copper, a more intense biologic action on the frog larvæ cannot be attributed to silver as secondary radiator with 3 mm. aluminum filtration, if the larvæ are placed close above the silver sheet.

It was deemed unnecessary to perform experiments on the human skin on account of the extensive analogy of the frog larvæ to the human skin as biologic test objects, and because these experiments had yielded only negative results.

*Observations on the Biologic Importance to the Human Skin of a Secondary Radiator Minutely Dispersed in the Biologic Object.*

As already mentioned, various salts of metals in aqueous or colloidal solution were brought to or in the human organ to be radiated to increase the biologic action of the X-rays in the proper place. The clinical results reported are anything but uniform, so that conclusions cannot be drawn. We have attempted to render the conditions somewhat simpler and have injected collargol in a circumscribed region of the skin, i.e., subcutis and subcutaneous tissue.

We then applied an erythema skin dose of X-rays filtered through 10 mm. aluminum to this region and as a control also to another homogeneous region of the skin which had not been injected.

We do not record the observations because the results were not uniform and did not agree with each other. Discrepancies are probably caused by the fact that collargol causes a mechanico-chemical irritation, at one time of a stronger and at another time of a lesser intensity, and thus the biologic action of the X-rays is interfered with. Further investigations are being conducted.

## Dependence of the Biologic Action on the Kind of Tissues. Sensibility Quotient

A biologic reaction in living tissue ensues from a lethal dose of X-rays and gamma-rays. Thereby the function of the radiated tissues is made to deviate from the normal. For instance, if we apply a known dose to the skin an irritation evidenced by an erythema appears as a visible deviation from the normal. The visible deviations of the application of a lethal dose of rays to the ovaries of a mature

woman are the cessation of ovulation and the arrest of menstruation.

The radiation dose which produces in the skin a visible erythema has been termed an erythema or skin dose. The radiation dose, which just suffices to cause in the ovary the cessation of ovulation and arrest of menstruation, has been named an ovarian dose.

Experience teaches that the same individual requires a different amount of radiation for the production of a skin dose than for the production of an ovarian dose. One kind of tissue does not show a change in the biologic function, while another kind of tissue evinces a distinct functional disturbance from a known dose. In the organism various kinds of tissues are adjacent to each other, and the X- or gamma-rays arising from a point source of radiation will send the same dose to the various neighboring tissues. However, a marked deviation in the behavior of absorption may be observed in the various kinds of tissues. One organ or tissue will evince a distinct functional disturbance, while the adjacent organ or tissue will not show any visible changes in function at all. This property of X- and radium-rays to produce with the same dose a marked functional change in one organ, while the other organ does not show any deviation from the physiologic function, is called the *elective action of rays.*

If we designate the dose which produces a distinctly visible reaction on the skin, i.e., an erythema with *a,* and the dose which causes a visible reaction in the ovary, i.e., an amenorrhea with *b,* we designate the quotient $\frac{a}{b} = \frac{\text{skin dose}}{\text{ovarian dose}}$ i.e., the quotient of sensibility between skin and ovary.

As the skin reacts quite readily and visibly to radiations, the erythema skin dose has been taken as the standard of comparison. Therefore, in the sensibility quotient the skin dose is always placed in the numerator, and the dose which is required to attain a desired biologic effect in another elementary tissue, in the denominator. If we wish to determine the sensibility quotient between skin and another elementary tissue according to this definition, it is only necessary to define what we understand by the desired biologic reaction.

The desired biologic reaction of the skin is known as an erythema of the first degree. The dose which produces this reaction is designated the skin dose, or erythema dose.

The desired biologic reaction of the ovary is the production of amenorrhea. The dose necessary to cause amenorrhea is called the ovarian dose.

The desired biologic reaction of carcinoma is the distinctly visible and palpable decrease in size of the carcinoma appearing after a certain time interval. The dose necessary to produce this reaction is termed the carcinoma dose.

If we place the size of the skin dose in relation to the size of the other mentioned doses, ovarian and carcinoma doses, and if we wish to determine the value of the different sensibility quotients, then the

difficulty is encountered that the skin dose which is placed in the numerator is subject to certain fluctuations in size in different individuals as well as in different skin regions of the same individual. The dose which produces upon the abdominal skin an erythema of the first degree is not equal to the dose which causes an erythema of the first degree on the skin of the sacral region. The skin of the sacral region is generally more sensitive to rays than the skin of the abdomen; the skin of the labia is ordinarily more sensitive than the skin of the abdomen. Altogether the differences are not very great. We found that the skin dose, measured with the ionization method, equals about 170 e if rays filtered with 3 mm. aluminum up to 1 mm. copper are used. We may in general accept this dose as the means for the skin dose in the calculation of the quotient of the dose.

As we shall see, the desired reaction for various other tissues in adult individuals is not subject to such great individual variations as seen in the skin. Therefore, the determination of the sensibility quotient $\frac{a}{b}$ for various elementary tissues is possible within certain limits. It is of such great importance that the approximate determination should be made.

*Determination of the Sensibility Quotient for the Ovary.*

To determine the size of this quotient it is necessary to compare those observations with each other in which, with the same quality of ray, the radiation dose has been approximately applied within the same time. The results may be obtained from those cited in the investigations of the law of Schwarzschild and the interval dose. The determination of the ovarian sensibility quotient became possible as soon as we were in a position to apply the ovarian dose with a given filter and a given technique within a single sitting. All earlier attempts to determine the sensibility quotient for the ovary were useless, owing to the necessity of obtaining the ovarian dose by several repeated radiations given within more or less extended time intervals. On account of individual differences, the number of cases for the determination of the sensibility quotient had to be large, as it must be in all biologic experimentation. The size of the skin dose was determined from a sufficiently large number such as 170 e. The ovarian dose can be likewise obtained from a correspondingly large number of cases. The method of the measurement of an ovarian dose was relatively simple in women, because we could insert the ionization chamber in the rectum at such a height that it came to lie in the immediate neighborhood of the ovary if the uterus was of normal size or slightly enlarged. If we radiate through the abdominal wall, observing a focus skin distance not too small and measuring the dose applied to the ovaries with the ionization chamber, we may consider the measured dose to be the ovarian dose. The ovarian dose wa

thus determined in a large number of hemorrhagic metropathies and small myomata. It was 33 e.

According to the above statement, the sensibility quotient of the ovary is calculated thus:

$$\frac{a}{b} = \frac{\text{skin dose}}{\text{ovarian dose}} = \frac{170}{33} = 5$$

In these determinations of the ovarian dose a filtration with 1 mm. copper was used, as it was much easier to obtain, with a radiation of this hardness, the ovarian dose in almost all cases through a single port of entry, and thus render the measurements relatively simple and exact. We also use in deep therapy filters of 3 mm. aluminum in thin women, on account of the economy and shorter duration of the radiation. Therefore, the question arises whether the sensibility quotient would change with the 3 mm. aluminum filtration in contrast to the copper filtration. According to our earlier investigations, the intensity of the biologic action of variously hard rays within the range of rays filtered with 3 mm. aluminum up to 1 mm. copper was the same. It was to be expected that the sensibility quotient obtained with a 3 mm. aluminum filtration would be the same as the one obtained with the harder filtrations. The proof had to be furnished. Difficulties were encountered, as with the use of these relatively soft rays the quotient of the dose between skin and ovary became very unfavorable to the skin. The dose necessary to obtain amenorrhea in one sitting could be applied to the ovary only in very lean women. We also had to use larger ports of entry. Only thus could we obviate all danger to the abdominal skin from the longer time duration of the radiation necessary.

The number of cases observed is therefore small. However, it is sufficiently large to permit of drawing conclusions. We radiated ten cases of hemorrhagic metropathies and myomatous uteri in this manner with 3 mm. aluminum, and determined the ovarian doses from the amenorrhea attained. The ovarian dose was about 35 e. The skin dose with this filtration is 170 e. We therefore may conclude:

The sensibility quotient of the ovary is about 5 when using X-rays filtered with 3 mm. aluminum.

*The Determination of the Sensibility Quotient of Carcinoma.*

To determine the size of this quotient $\frac{\text{skin dose}}{\text{carcinoma dose}}$ we may refer to the preceding statements concerning the skin dose which had been placed at 170 e.

By carcinoma dose we understand the dose which causes a carcinoma to retrogress decidedly, so that it either disappears or

appears to be reduced in size as determined by the senses of sight and touch.

To avert misinterpretations we desire to expressly mention that the disappearance of the carcinoma to the senses of sight and touch after the application of the radiation dose is not at all identical with a cure. We do not speak of a cure after the operative removal of a carcinomatous tumor, and we are not permitted to speak of a cure after retrogression of a carcinoma by radiation, because in both instances experience teaches that recurrences of the carcinoma may occur. Just as in the determination of the sensibility quotient of the ovary, so the determination of the sensibility quotient of carcinoma became possible as soon as we were placed in a position to attain the cancer dose in one sitting by an efficient filtration and a correct technique. This was possible in certain carcinomata, as we have seen. Yet special difficulties are encountered in the determination of the carcinoma dose in contrast to that of the ovarian and skin doses. We saw that the ovarian and erythema dose did not perceptibly deviate from a mean, excepting a few isolated instances. If we now apply in an analogous manner a certain definite dose to a carcinoma, we see that in one case the tumor completely disappears to the senses of sight and touch, while in another case a retrogression can hardly be observed; on the contrary, the carcinoma continues to progress. Pronounced individual fluctuations, therefore, are met with in the carcinoma dose. Upon what these large individual fluctuations are dependent is still beyond our comprehension. We may surmise that the varying histologic structure of the carcinoma causes this varying behavior to the X-rays, a view which Adler has even recently pronounced. Almost all our radiated carcinomata were examined in the pathologic institute of Freiburg. We have not so far been able to recognize definite relations between the histologic structure of carcinomata and the action of X-rays. We have observed a distinct difference in the behavior to rays, according whether the carcinoma bearer is or is not cachectic. For instance, if we ray a mammary cancer, which has involved the glands or has formed metastases in other organs, we can apply a far larger dose than the established mean cancer dose without a perceptible retrogression in the carcinoma taking place.

Another difficulty in the determination of the carcinoma doses arises, then, if we apply the cancer dose to a deep-seated carcinoma. To attain at this place the mean carcinoma dose we must apply to the tissues lying above it a relatively high roentgen dose. As a result of this X-ray radiation a permanent injury to the general health of the patient often occurs, which we call an X-ray cachexia on account of its great resemblance to the clinical picture of cancer cachexia. In such women we did not see a retrogression of the carcinoma in spite of the application of a much higher dose than the mean carcinoma dose.

All such cases have been excluded from the determination of the carcinoma dose on account of the difficulties mentioned. We have exclusively used those cases of mammary carcinomata in the determination of the lethal carcinoma dose, in which the carcinoma had not yet assumed a large extent, in which metastases in other organs could not be demonstrated clinically, and in which large glandular tumors in the axilla or supraclavicular regions could not be recognized. The conditions for the determination of the carcinoma dose were especially favorable in these cases, because we could measure with the measuring chamber the doses applied to the carcinoma, and because we did not need to administer at the same time large X-ray doses to the adjacent normal tissues on account of the relatively superficial location of the cancer. A filtration of the X-ray through 1 mm. copper was employed in the determination of the carcinoma dose. The focus skin distance was 50 cm. Thus we obtained an impregnation of the carcinoma with X-rays as uniform as possible. Referring to the cases of mammary cancer mentioned on page 137, and observing all the limitations discussed above, the results obtained revealed that the cancer exhibits an extensive retrogression up to a complete disappearance to the senses of sight and touch when, with a single radiation, a mean dose of about 150 e has been applied. As the erythema dose with the use of a 1 mm. copper filtration is 170 e, the sensibility quotient for mammary carcinoma is:

$$\frac{a}{b} = \frac{\text{skin dose}}{\text{carcinoma dose}} = \frac{170}{150} = 1.15$$

As we based the determination of the mean carcinoma dose exclusively on mammary cancers, we do not wish to tacitly imply that carcinomata localized in other regions will not react to the same dose. To prove that carcinomata localized in other regions also completely disappear to the senses of sight and touch with this dose, we give the following clinical histories:

Case Mrs. M., carcinoma capitis, 52 years old. On the scalp a broken-down tumor about the size of a fist is found, about 12 cm. in diameter and 3 cm. in height. (See table XXX, fig. 1.) Diagnostic excision. Histologic diagnosis of the pathologic institute in Freiburg reveals cornifying squamous epithelial cell carcinoma.

*Days of radiation:* Sept. 13 and 14, 1916.

Radiation with Coolidge tube. Focus skin distance 50 cm., 1 mm. copper filtration, dose 140 e. Size of field selected so large that the entire tumor is placed within the radiation beam.

Sept. 21, 1916—Tumor has disappeared completely. A granulating area is seen the size of a quarter in place of the growth. (See table XXX, fig. 2.)

Case Mrs. S., carcinoma vulvæ, 58 years old. Starting from the clitoris and invading to the left the small and large labia, a large carcinomatous ulcer is seen. (See table XXXI, fig. 1.) Urethra and inguinal glands are not involved. The histologic diagnosis of the pathologic institute in Freiburg reveals a carcinomatous new growth.

*Day of radiation:* Aug. 22, 1916.

Radiation with Coolidge tube. Focus skin distance 50 cm., 1 mm. copper filtration, dose 100 e.

Oct. 2, 1916—Carcinomatous ulcer is completely healed; the skin is somewhat reddened. (See table XXXI, fig. 2.) General health good, glands free.

Dec. 20, 1916—The findings are the same.

## On the Dependence of the Intensity of the Biologic Action with the Same Dose from the Individual

In our comparative animal experiments we had already observed that the animals did not at all react evenly to the same dose. Differences were seen in the timely occurrence as well as in the intensity of the radiation symptoms. The mortality as a result of the action of the rays differed within certain limits. We attempted to reduce the disturbing factor found in the different individuals by using a large number of experimental animals, and further by selecting experimental animals of the same parentage and the same litter. Nevertheless, a certain individual difference existed which can best be expressed in numbers by determining the difference in the mortality from the known time intervals after radiation and the percentual frequency of the radiation symptoms at successive observations.

We may refer to the protocols, reported in the preceding chapters, from which it follows that with the application of the same X-ray dose to a frog-spawn clump of the same litter the characteristic X-radiation disease and the characteristic X-ray deaths appear in the different individuals in varying degrees and at different time intervals. To determine these individual differences in numbers we have performed several experiments in which we counted within regular time intervals in a known number of animals those that succumbed to the radiation disease and those that evinced radiation symptoms. We will here report a few extracts from the observation journal:

In one series of experiments one hundred frog larvæ were radiated with a dose of 60 e and a 3 mm. aluminum filtration.

It was recorded on the seventh day following the radiation that all the one hundred animals were alive, that thirty-two of them evinced symptoms of radiation disease, while sixty-eight did not show any visible reaction.

It was recorded fourteen days after radiation: eighty animals are still living; twenty died from symptoms of radiation disease. Twenty-five of the surviving animals have symptoms of the radiation disease.

Twenty-four days after radiation, thirty-five animals are still alive; all evince the symptoms of radiation disease.

Another series, in which the same number of experimental animals was radiated, but this time with 80 e, gave the following report:

The sixth day after radiation: All animals are living; eight show distinctly marked symptoms of radiation sickness.

Thirteenth day after radiation: Ninety-four animals are still alive; fifty have characteristic symptoms of radiation disease.

Sixteenth day after radiation: Forty-three animals are still alive. They all show the symptoms of radiation disease.

Twenty-ninth day after radiation: Two animals are still living.

We see from these experiments that the degree of the reaction differs in time of occurrence as well as in intensity, even in individuals of the same litter and of the same age. Observations made in some of the experiments we must especially mention. In the same litter of the same age and exposed to very large doses, one or more individuals may be seen which do not show any signs of radiation sickness; yes, even evince an essentially more rapid growth than the controls even within a longer period of observation; while all the other animals rapidly succumbed to the large radiation dose. To give somewhat of an idea of the quantitative differences of the doses applied, we mention an experiment in which the one surviving animal received double the dose, while half the dose was sufficient to kill all the others in a short time with the characteristic signs of the Roentgen disease.

If, therefore, some roentgenologists claim that the sensibility of single individuals may fluctuate within limits of plus or minus ten, or even within twenty per cent, and others state that a pronounced increased or lowered sensibility does not exist, we could demonstrate in individuals of the same species, of the same litter and the same age, a lowered sensibility of at least 100 per cent in reference to the death dose.

In deep therapy the radiations must be given to human beings of varying ages and varying descent. As marked analogous behavior to X-rays exists between the biologic test object and human tissues, we had to expect at the outset that pronounced decreased and increased sensibilities also exist in the human. As we did not radiate the entire organism, we had to confine our observations on the individual differences to tissues of the same kind. We previously called attention to the individual differences seen in experimental animals, and surmised that the same observation would be made in human tissues.

The degree of the individual differences acquires practical importance, as we must attempt to avoid dangerous under- or overdosation in deep therapy. The limitations of the dose, to be observed in the attainment of a desired biologic action, are relatively slight. If very marked individual differences in the reaction of the same kinds of tissues to the same mean dose did exist in the human, then we would obtain a certain percentage of undesired over- and under-dosations in deep therapy. It is therefore important to gain a clear conception of the different behavior of like tissues to applications of the same dose in different human beings.

We will consider in these observations three kinds of tissues:

1. Skin,
2. Ovary,
3. Carcinoma.

We are absolutely justified to determine an average erythema skin dose based on results obtained in a large number of cases, and we determined the mean erythema dose as 170 e.

The question whether this dose may exceptionally produce in different individuals a much stronger or weaker biologic reaction on the skin has been differently answered. Some believed, basing their opinions chiefly on the method of the Kienböck measurement and other radio-chemical methods of measuring, that a difference in the degree of the reaction of the skin should be admitted, but within very narrow limits, while others maintain that wide variations in the reaction of the skin exist, particularly when using X-rays.

The arguments which have been advanced to uphold these views are not at all tenable. The authors usually confined themselves to the statement that an individual oversensitiveness of the skin could not be assumed, for they had never seen in their "X-ray practice" a "burning" of the skin.

It is hardly necessary to say that such a method of proof is weak, and we would not enter upon a discussion if such a forensic opinion, even if made by an authority, could not influence a legal declaration in one or another direction. The authors, who have so far not seen any skin burns, and therefrom drew this wrong conclusion, have applied X-ray doses to the skin which are far below the erythema dose. They have only practiced X-ray diagnosis or X-ray therapy in tumors as myomata, which are easily influenced. In a simple diagnostic fluoroscopic or radiographic radiation, scarcely one-tenth of the erythema dose will be attained during several exposures, even when using thin aluminum filters. If we treat myomata with the multiple field method of radiation of Gauss and Lembke, not even one-half of the erythema dose is obtained, if we observe their directions to give only 30 x-Kienböck units as skin dose. Accordingly, injuries of the skin are not observed with such decided underdosations. Such procedures cannot serve as proof that a pronounced individual difference in the reaction does not exist. Even with this pronounced underdosation, Gauss and Lembke could demonstrate that in certain individuals of the so-called titian teint erythemata, though of milder degrees, could be attained. We may, therefore, state that individual oversensitivenesses of 100 per cent are observed. A correct dosation cannot be made with radio-chemical methods of measurement.

We could at times observe quite marked deviations in the reactions of the skin to a mean dose even with the use of the much more exact method of ionization measurement. They consisted of an undersensibility as well as an oversensibility. As we have already cited an example of oversensibility, we also desire to relate examples of exceptionally pronounced undersensibility. The latter is frequently observed in very old, decrepit and markedly cachectic

individuals. A certain definite law seems to prevail in such instances. As the carcinoma in such cachectic individuals does not respond to the lethal carcinoma dose, we have, with the permission of the patient, applied a much higher dose to the skin lying above the carcinoma. Thus we applied in two cases double the dose—300 e—a dose which would produce in the normal skin burn of the second to third degree with the formation of vesicles and necrosis. Only a slight browning of the skin was observed in these cases.

Therefore, an undersensibility of 100 per cent exists in these cases. Such a result should not surprise us. In the simplest unicellular living organisms, the bacteria, a varying reaction to the same doses of chemical reagents is observed in the different individuals ranging within one to many hundreds per cent, and credit cannot be attached to the statement of roentgenologists that the skin should biologically possess an entirely different behavior to the X-rays. It is self-evident, without giving further proof, that isolated instances of over- and undersensibility of the skin to rays do exist. These differences will fluctuate not within the range of a few per cent, but within limits of 200 to 300 per cent. In order not to be misunderstood, we desire to again remark that these exceptional over- and undersensibilities are the exception, and they should not hinder us from drawing binding conclusions from the gross of the observations.

The second kind of tissue in which we could investigate the dependence of the intensity of the biologic action from the individual was the ovary. The intensity of the biologic action was incidentally tested during the radiation treatment of myomata. We spoke of ovarian dose then when a dose was applied to the ovary which produced an amenorrhea. In the methods of radiation treatment of myomata employed hitherto the ovarian dose was not determined directly but indirectly from the doses applied to each port of entry in the multiple small field method mostly used. The Kienböck strips or other radio-chemical methods were ordinarily used in this procedure, the inaccuracy of which has already been emphasized. One added the Kienböck x-units applied to the different skin areas and stated that amenorrhea appeared with 500 X. It is evident that with such methods the dose cannot be determined which the ovary received during the radiation.

In the different patients according to the state of nourishment a variously thick layer of tissue had to be traversed first by the X-rays, which reduced the intensity of the radiation more or less, before they reached the ovary. In the multiple small field method, which is based on crossfiring, it was not always possible to place the ovaries exactly within the radiation beam. Finally it may be noted that the number of ports of entry was different with the different therapeutists, whereby the error in the deductions was rendered still larger. We therefore should not be surprised that

the statements on the number of X employed to produce amenorrhea, fluctuate within enormous limits. While some attained amenorrhea with 500 X, others obtained it with 2000 X and more, although the same number of fields were used. In spite of these great fluctuations in dose, with which the various authors obtained amenorrhea it is noteworthy that almost all authors have formed quite definite opinions on the dependence of the ovarian dose from the individual.

The individual variations of the ovarian dose were thought to be dependable on the age of the patient. The opinion is almost general that the older a woman is, the more her ovaries approach the atrophic stage of the climacteric, the easier the ovaries may be disabled by radiations.

Albers Schönberg promulgates eight conclusions in his treatise, "Ergebnisse der Roentgentherapie bei Myoma," 1913. The first sentence and the eighth interest us especially.

"1. The ovaries sustain through the X-rays an atrophy mainly in the Graafian follicles. As a result an artificial menopause occurs. The damage appears rapidly and permanently in older women that approach or are in the climacteric years. The intended atrophy of the follicles is attained only after a much longer radiation in younger individuals at the beginning of the fortieth year of life.

"8. Myomata of younger women (below 40 years) are generally not so well adapted for radiation. The older the woman, the more promising is the roentgen treatment."

Eymer and Menge draw the following conclusions from their labors, reported in the "Monatschrift fur Geburtshülfe und Gynäkologie," 1912, 3:

"It is seen from the study of our cases that in women above forty years we are well able to render them permanently amenorrhoic, and in women between thirty and forty to attain a pronounced oligomenorrhea. We may safely attain an amenorrhea in younger women also, but this is only possible after a radiation composed of many series. However, this is not advisable, except in myomata." And further: "With increasing age a decreasing X-ray dose is generally necessary, which also holds good for the hemorrhagic metropathies."

Heimann, also, states in his publication in the "Berliner Klinische Wochenschrift," 1916, No. 37: "Young women require a larger amount of radiation for the production of amenorrhea than older ones."

Runge, Berlin, states in the supplements of the "Medizinische Klinik," 1912, No. 12: "The success of X-rays depends in the first place on the age of the patient." He deduces that it is not correct to radiate young myoma patients below thirty to thirty-five years with X-rays. For in spite of the most intensive radiation it would not be always possible to produce amenorrhea in such cases.

Almost all the other authors, who have taken sides in this question, express themselves in the same sense.

tematic investigations and observations are required for it. The presumptions, with which we must be contented at present, have already been expressed in the chapter on the determination of the sensibility quotient for carcinoma.

We refer here again to these observations.

# APPENDIX

## EXPERIMENTAL INVESTIGATIONS OF THE INFLUENCE WHICH THE FOCUS SKIN DISTANCE AND THE SIZE OF THE FIELD HAVE ON THE QUOTIENT OF THE DOSE [1]

BY WALTER FRIEDRICH AND HANS KORNER

One of the most important questions in radiation therapy is that of the size of the quotient of the dose, i.e., the ratio of the depth dose to the surface dose. This ratio depends upon the distance of the radiation source from the surface and upon the depth of the radiated object; upon the absorption of the rays (half absorption value layer) in the radiated tissue, and finally upon the scattered radiation in the tissue. The influence of distance and absorption on the quotient of the dose may be calculated by means of the law of squares and the absorption coefficient.

The third factor—the scattered radiation of the radiated tissue area—has not been considered in such calculations. The great influence of the scattered rays on the dose and on the distribution of the dose was emphasized, perhaps for the first time, by Kroenig and Friedrich in 1915.[2]

Scattered rays can only arise in a medium which possesses an absorption coefficient for X-rays, as the formation of them is a secondary process due to a scattering of a part of the primary rays. The formation of the scattered radiation therefore is dependent on the kind of primary radiation and the kind of object which is radiated. If one assumes in a given case, with a known quality of rays and a known radiated medium, that this medium is infinitely large, and assumes further a fixed point at sufficient depth within this medium, then this point receives a maximum of scattered rays from all sides.

The conditions, however, are different if the point instead of being located sufficiently deep is situated at the periphery of the area where it borders on another area that is traversed by rays which have not formed secondary rays. In this instance the point will not receive any scattered radiation from the second medium. Quite similar are the conditions if the medium, in which the scattered radiation arises, is not infinitely large as in the first instance

[1] Strahlentherapie, Vol. XI, 1920.

[2] W. Friedrich and B. Kroenig, Münch. Med. Wochenschr., 1915, No. 49.

but, for example, represents an irradiated truncated pyramid in the body substance, the size of which is determined by the size of the square port of entry on the skin and by the distance of the anticathode of the X-ray tube from the body surface and by the altitude of the pyramid. Here also the maximum of scattered radiation at a given point is attained only if the point lies as centrally as possible.

On the other hand, one will approach the more closely the values calculated from the law of distance and the half absorption value layer of the rays, the smaller the radiation cone is which is sent through the medium. The correctness of this theoretical hypothesis has already been experimentally proven by the researches of

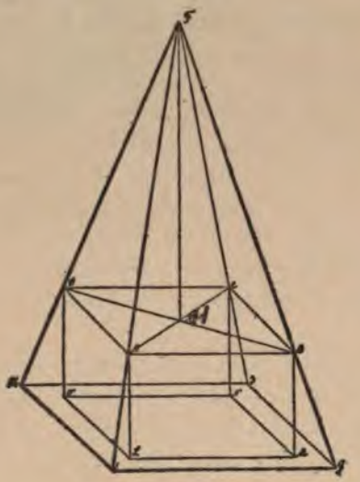


FIG. 64.

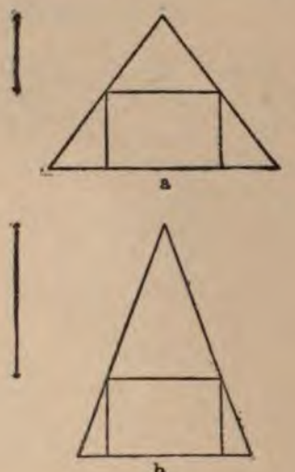



FIG. 65.

FIG. 64.—The anticathode is assumed to be at F. The pyramid F E G J K represents the area traversed by the X-rays. A B L D is the port of entry. F H is the focus skin distance. The truncated pyramid A B L D F G J K represents the area of the radiated body tissue. A B L D L M N O is the central block; the prisms lie adjacent to it.

FIG. 65 represents a section placed through the axis of the pyramid and the centers of two opposing corners of the base for varying F H. In Fig. 65, b, the F H is twice as large as in Fig. 65, a. The central block remains the same, while the prisms adjoining laterally decrease in size with an increase in F H.

Kroenig and Friedrich,[1] and has been confirmed by the investigations of Seitz and Wintz, Dessauer and Warnekros, and Glocker. They showed that the dose in the deep increases with the increase in the size of field, while the values calculated from the laws of distance and absorption are independent from the size of the field. In other words, the quotient of dose becomes more favorable with an increased size of the field. The experimental investigations of Kroenig and Friedrich conducted so far have taken into account the various sizes of fields with a known hardness of ray, without con-

[1] Kroenig and Friedrich, Physikalische und biologische Grundlagen der Strahlentherapie. Berlin, 1918. English Translation, Rebman Co., New York, 1922.

sidering the distance of the anticathode from the skin surface. This distance of anticathode from skin surface we will designate as F. H. in the following parts of the paper. We have undertaken in this report to systematically investigate in the deep layers of the radiated medium the following factors: hardness of rays, size of field, and focus skin distance (F. H.).

If our theoretical hypotheses are correct, then we must expect with an increase in F. H., the field size and the radiation hardness remaining the same, a correspondingly smaller decrease of the dose in the depth according to the laws of squares and absorption. One must, however, realize that if with various F. H. the port of entry is kept constant, the radiated body volume is not of the same size. If with a square port of entry the radiated body volume presents a truncated pyramid, then the pyramid is composed of (1) a central square block, whose base is fixed by the port of entry and whose height is equal to the altitude of the truncated pyramid; and (2) four prisms located laterally from the central block (Fig. 64). The volume of the central block remains constant with a constant size of port of entry but different F. H., but the size of the prisms changes essentially so that they are larger with short F. H. and shorter with long F. H.

These conditions are best realized by studying Fig. 65, which represents a section through two such radiation cones.[1] This means for our conception of scattered radiation that with a short F. H. we have a large addition of scattered radiation corresponding to the greater mass of the radiated volume, and with a large F. H. only a small addition. In other words, with a constant size of field and constant hardness of rays and with short F. H. the primary radiation at a known depth determined by the laws of distance and half absorption value layer is relatively small and the addition of scattered radiation is relatively large. With a large F. H. the primary radiation is larger and the scattered radiation is smaller in proportion. To prove these confusing conditions purely by calculation appeared to be impractical and therefore the experimental method was employed as described on page 10.

The first experiments were conducted with a Coolidge tube activated with an inductor and gas interrupter (Sanitas apparatus). The tube was activated by a current with a voltage having a parallel spark-gap of 38 cm., the hot cathode was charged from a storage battery of 3.5 to 4 ampères. The tube was placed in a holder consisting of thick leaded glass and placed above the phantom so that the central ray from the anticathode struck the ionization chamber. The tube was usually charged with 2 mamp. A lead diaphragm was placed underneath the tube bowl which also served as the seat for the various filters. The diaphragm which formed the proper limits

[1] Similar relations are naturally present in radiation cones of circular as well as rectangular transverse sections.

of the radiation field was placed directly above the phantom. (See Fig. 66.)

The apparatus was distributed into two neighboring rooms so that the inductor, interrupter, tubestand and tubes, phantom and ionization chamber were in one room and the electrometer and control table in the other. The second room was separated from the other by the wall between the rooms and a heavy lead door 10 mm. thick. During the first measurements it was found that the intensity of the radiation emitted from the Coolidge tube was subject to quite widely varying fluctuations due to fluctuations in the

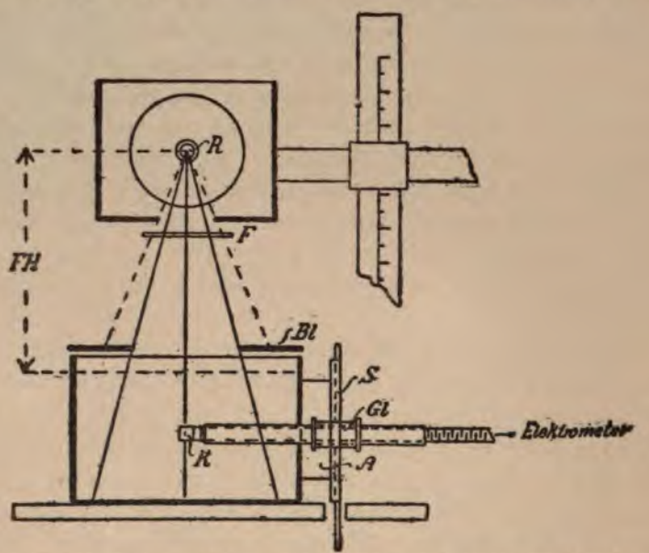



FIG. 66.—Arrangement of tubes, filters, water phantom and ionization chamber.

city current. Therefore the measurements were performed during the night hours. However, the same fluctuations were observed. They were finally obviated by placing a regulator resistance in the circuit, by means of which we were enabled to maintain a constant current by the control of the voltmeter and by regulation of the resistance. Thus it was possible to maintain the intensity of the radiation perfectly constant even with a long-continued series of experiments.

The time was measured within which the electrometer leaf, after charging the electrometer, would pass through five divisions of the scale. The reading of the electrometer was done with a small microscope. As the discharge times of the electrometer with a constant tube intensity are in an indirect ratio to the dose attained at variable places, the intensity of the dose could thus be determined. The electrometer system was kept charged for at least one to two hours prior to each measurement to exclude losses of electric current by polarization of the dielectric during the progress of the measurements.

The technique of the measurements was conducted so that after alignment of the measuring chamber and anticathode, regulation of the field size, adjustment of the F. H., insertion of filter and regulation of tube, the entire radiation area was protected from the direct rays by a lead filter 10 mm. thick. The time of the discharge of the electrometer leaf for five divisions of the scale was then determined. As the measuring chamber and the region to be radiated were thus well protected from the direct rays, only the scattered radiation arising from the walls and objects in the room could act upon the measuring apparatus. This radiation has been termed "the undesired radiation." It was always measured and taken into account in the calculation of the final results.

For comparison of the measured dose values with each other, the dose measured at the surface was always placed at 100 and the doses measured in depths of 1 to 10 cm. were expressed in percentages of the surface dose.

After some preliminary experiments we began with systematic measurements using a port of entry of 14 cm. square. We determined the doses in depths of 0, 2, 4, 5, 6, 8 and 10 cm. The distances of the anticathode from the port of entry (F. H.) were 25, 30, 35, 40, 45 and 50 cm. The X-rays were filtered either with 10 mm. aluminum or 1 mm. copper. The X-rays were generated in a Coolidge tube operated with a voltage having a 38 cm. parallel spark-gap. After determining the time consumed for the undesired radiation, the discharge times at the designated depths were determined. Then columns of observations were made for each field. They were obtained so that in the first series the discharge times at 10, 8, 6, 5, 4, 2 and 0 cm. depth were determined in sequence; in the second at 0, 2, 4, 5, 6, 8 and 10 cm., and in the third at 10, 8, 6, 5, 4, 2 and 0 cm. Two readings were made for each point to eliminate, as far as possible, any errors in the individual readings. The mean of the values found was then taken and the time of the undesired radiation was entered in the calculations. The dose at 0 cm. was considered 100. Finally the doses for the other distances were determined in per cent of the 0 cm. dose from the corrected time values. The tables and curves give the best survey of the experiments.

To deduce from the tables how large the influence of the scattered radiation on the dose for the different field sizes and focus skin distances is, we determined the half absorption value layer for both the hardnesses of rays used in these investigations. We then calculated from the laws of squares and the half absorption value layer the degree of decrease of the dose within the deeper layers without considering the additional intensities obtained from the scattered rays.

We determined the half absorption value layer, avoiding as far as possible any scattered radiation and obtained a half absorption

value layer of 2.9 cm. in water for X-rays filtered with 10 mm. aluminum, and 3.3 cm. in water for X-rays filtered with 1 mm. copper.[1]

The calculated values for the decrease of the dose obtained from the law of squares and the half absorption values determined are recorded in the table under the first columns.

TABLE I.

Port of entry: 14 x 14 cm, 10-mm-Aluminum-Filter.

Measured and calculated values of dose

| Distance in cm. | FH=25 cm | | FH=30 cm | | FH=35 cm | | FH=40 cm | | FH=45 cm | | FH=50 cm | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 81.3 | 53.2 | 79.7 | 54.3 | 82.2 | 55.5 | 87.7 | 56.2 | 88.2 | 56.9 | 84.2 | 57.4 |
| 4 | 59.9 | 28.6 | 58.6 | 29.9 | 70.0 | 30.9 | 69.3 | 31.8 | 69.0 | 32.4 | 62.7 | 32.9 |
| 5 | 51.4 | 21.1 | 52.9 | 22.3 | 59.8 | 23.2 | 60.2 | 23.9 | 58.1 | 24.5 | 55.4 | 25.1 |
| 6 | 43.8 | 15.5 | 44.2 | 16.6 | 51.1 | 17.4 | 52.3 | 18.1 | 49.0 | 18.6 | 47.6 | 19.0 |
| 8 | 29.1 | 8.5 | 32.3 | 9.2 | 35.9 | 9.8 | 37.9 | 10.3 | 36.6 | 10.7 | 34.7 | 11.0 |
| 10 | 22.1 | 4.7 | 23.1 | 5.2 | 25.5 | 5.6 | 25.7 | 5.9 | 26.2 | 6.2 | 25.7 | 6.4 |

TABLE 2.

Size of field: 14 x 14 cm, 1-mm-Copper-Filter.

| Distance in cm. | FH=25 cm | | FH=30 cm | | FH=35 cm | | FH=40 cm | | FH=45 cm | | FH=50 cm | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 81.8 | 56.3 | 87.4 | 57.5 | 86.5 | 58.8 | 86.1 | 59.4 | 88.7 | 60.2 | 90.8 | 60.8 |
| 4 | 68.3 | 32.2 | 71.1 | 33.7 | 72.5 | 34.7 | 74.5 | 35.3 | 69.1 | 36.5 | 76.1 | 37.0 |
| 5 | 59.2 | 24.3 | 63.8 | 25.7 | 64.5 | 26.8 | 62.0 | 27.6 | 63.9 | 28.4 | 68.9 | 29.0 |
| 6 | 52.3 | 18.5 | 54.6 | 19.7 | 56.7 | 20.7 | 51.8 | 21.6 | 58.2 | 22.1 | 57.0 | 22.6 |
| 8 | 38.0 | 10.7 | 39.8 | 11.6 | 41.0 | 12.3 | 40.2 | 12.9 | 41.6 | 13.4 | 45.6 | 13.8 |
| 10 | 27.9 | 6.2 | 28.2 | 6.9 | 30.2 | 7.4 | 31.2 | 7.8 | 32.4 | 8.2 | 33.7 | 8.5 |

(The graphs of the values for FH=25, 35, 50 and 1 mm. copper filtration are shown in Fig. 67.

For a field size of 14 x 14 cm. an increase of F. H. from 25 to 50 and X-rays filtered with 10 mm. Al., gives an increase of the dose from 22.1% to 25.7% at a depth of 10 cm. in water; and for rays filtered with 1 mm. copper a corresponding increase from 27.9% to 33.7%. Previously we had explained that with a change of F. H. (with the same size of field and the same hardness of rays) the action of the laws of squares is directly the opposite of that of the scattered rays. As the influence of the hardness of the rays (the absorption coefficient) is independent of the field size, the hardness of the rays may be excluded from these considerations. The experimental investigation has shown that for a field of 14 cm. square the law of squares is the determining factor, for with an increase in F. H. the depth dose has increased.

[1] The difference of these values for the half absorption value layer from those given by Krönig and Friedrich may be explained by the fact that in the details of these experiments the influence of the scattered rays found in the radiated water was not as completely excluded as in the present methods.

In order to further investigate experimentally our conception of the connection of the three factors which influence the dose—the law of distance, the half absorption value layer, the scattered radiation—and if possible, to obtain laws relating to them and the F. H. and field size, we changed the sizes of the ports of entry and subjected fields of 2, 8, and 10 cm. square to systematic investigations. The differences in the values must of course be attributed to the variable intensity of action of the scattered rays as neither the laws of squares nor of the half absorption value are influenced by the field size. Based on the investigations of Krönig and Friedrich, we must expect for the smaller fields (2 x 2 and 8 x 8 cm.) a steeper course of the graph of the dose and for the field 20 x 20 cm. a correspondingly more sloping course of the graph than shown in the graph determined for the field 14 x 14 cm.

TABLE 3.

Size of field: 2 x 2 cm, 10-cm Aluminum Filter

| Distance in cm | Measured and calculated values of dose | | | | | |
|---|---|---|---|---|---|---|
| | FH=25 cm | | FH=35 cm | | FH=50 cm | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 63.9 | 53.2 | 72.0 | 55.5 | 66.9 | 57.4 |
| 4 | 40.6 | 28.6 | 42.3 | 30.9 | 42.2 | 32.9 |
| 5 | 30.7 | 21.1 | 34.2 | 23.2 | 34.9 | 25.1 |
| 6 | 24.0 | 15.5 | 26.0 | 17.4 | 26.7 | 19.0 |
| 8 | 15.9 | 8.5 | 17.0 | 9.8 | 16.5 | 11.0 |
| 10 | 10.1 | 4.7 | 10.3 | 5.6 | 10.9 | 6.4 |

TABLE 4.

Size of field: 2 x 2 cm, 1-mm-Copper-Filter

| Distance in cm | Measured and calculated values of dose | | | | | |
|---|---|---|---|---|---|---|
| | FH=25 cm | | FH=35 cm | | FH=50 cm | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 67.1 | 56.3 | 62.9 | 58.8 | 71.9 | 60.8 |
| 4 | 42.6 | 32.2 | 42.8 | 34.7 | 47.7 | 37.0 |
| 5 | 34.4 | 24.3 | 34.3 | 26.8 | 38.4 | 29.0 |
| 6 | 27.6 | 18.5 | 27.9 | 20.7 | 29.1 | 22.6 |
| 8 | 18.3 | 10.7 | 19.1 | 12.3 | 18.7 | 13.8 |
| 10 | 12.1 | 6.2 | 12.4 | 7.4 | 12.4 | 8.5 |

TABLE 5.

Size of field: 8 x 8 cm, 10-mm-Aluminum Filter

| Distance in cm | Measured and calculated values of dose | | | | | |
|---|---|---|---|---|---|---|
| | FH=25 cm | | FH=35 cm | | FH=50 cm | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 79.4 | 53.2 | 79.6 | 55.5 | 80.5 | 57.4 |
| 4 | 58.8 | 28.6 | 61.2 | 30.9 | 58.9 | 32.9 |
| 5 | 49.7 | 21.1 | 50.8 | 23.2 | 52.0 | 25.1 |
| 6 | 39.9 | 15.5 | 42.2 | 17.4 | 42.8 | 19.0 |
| 8 | 27.8 | 8.5 | 29.2 | 9.8 | 31.2 | 11.0 |
| 10 | 19.4 | 4.7 | 20.9 | 5.6 | 22.8 | 6.4 |

TABLE 6.

Size of field: 8 x 8 cm, 1-mm-Copper-Filter

| Distance in cm | Measured and calculated values of dose | | | | | |
|---|---|---|---|---|---|---|
| | FH=25 cm | | FH=35 cm | | FH=50 cm | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 78.0 | 56.3 | 84.9 | 58.8 | 82.0 | 60.8 |
| 4 | 54.9 | 32.2 | 58.0 | 34.7 | 64.5 | 57.0 |
| 5 | 48.2 | 24.3 | 51.4 | 26.8 | 57.9 | 29.0 |
| 6 | 41.2 | 18.5 | 43.2 | 20.7 | 48.2 | 22.6 |
| 8 | 29.2 | 10.7 | 31.8 | 12.3 | 35.6 | 13.8 |
| 10 | 21.5 | 6.2 | 23.0 | 7.4 | 26.2 | 8.5 |

TABLE 7.

Size of field: 20 x 20 cm, 10-mm-Aluminum-Filter

| Distance in cm | Measured and calculated values of dose | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | FH=30 cm | | FH=35 cm | | FH=40 cm | | FH=50 cm | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 84.6 | 54.3 | 88.8 | 55.5 | 86.1 | 56.2 | 87.8 | 57.4 |
| 4 | 65.9 | 29.9 | 64.2 | 30.9 | 70.0 | 31.8 | 67.8 | 32.9 |
| 5 | 57.8 | 22.3 | 57.8 | 23.2 | 59.6 | 23.9 | 59.8 | 25.1 |
| 6 | 47.7 | 16.6 | 51.0 | 17.4 | 51.8 | 18.1 | 52.9 | 19.0 |
| 8 | 35.0 | 9.2 | 38.0 | 9.8 | 39.0 | 10.3 | 41.5 | 11.0 |
| 10 | 26.1 | 5.2 | 28.1 | 5.6 | 29.6 | 5.9 | 31.2 | 6.4 |

TABLE 8.

Size of field: 20 x 20 cm, 10-mm-Copper-Filter

Measured and calculated values of dose

| Distance in cm | FH=30 cm | | FH=35 cm | | FH=40 cm | | FH=50 cm | |
|---|---|---|---|---|---|---|---|---|
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 88.8 | 57.5 | 85.8 | 58.8 | 91.3 | 59.4 | 93.0 | 60.8 |
| 4 | 75.2 | 33.7 | 70.2 | 34.7 | 73.9 | 35.3 | 82.0 | 37.0 |
| 5 | 66.5 | 25.7 | 62.9 | 26.8 | 66.2 | 27.6 | 73.8 | 29.0 |
| 6 | 56.6 | 19.9 | 56.2 | 20.7 | 58.0 | 21.6 | 69.1 | 22.6 |
| 8 | 43.5 | 11.6 | 49.9 | 12.3 | 47.2 | 12.9 | 54.1 | 13.8 |
| 10 | 33.6 | 6.9 | 34.6 | 7.4 | 37.9 | 7.8 | 41.4 | 8.5 |

The following illustrations show the graphs for the values recorded in the tables, Fig. 67, for the field sizes 2 x 2, 8 x 8 and 14 x 14, 1 mm. copper filtration and a F. H. of 25, 35 and 50 cm.; and Fig. 68 for a field size of 20 x 20 cm., a 10 mm. aluminum, as well as a 1 mm. copper filtration and a F. H. of 30, 35, 40 and 50 cm.

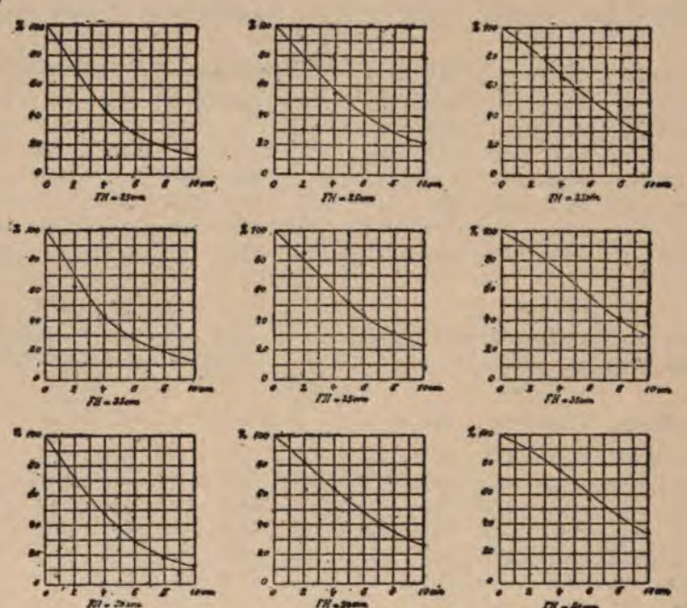


FIG. 67.—Decrease of the dose in the deep with 1 mm. copper filter and F.H. of 25, 35 and 50 cm. and field sizes 2 x 2 cm., 8 x 8cm. and 14 x 14 cm.

The results of the investigations show that our theoretical explanations have been entirely confirmed. The graph of intensity drops steepest in the smallest field investigated (2 x 2 cm.), and slowest in the largest field (20 x 20 cm.). The dose in the depths grows larger in all the field sizes with an increasing F. H. The increase is only a small one in the small fields, and pronounced in the larger fields.

It is seen that the values found for the small fields, particularly

the size 2 x 2 cm., closely approach the calculated values. With a field size 0 the calculated values would coincide with the experimental values and vice versa; with large fields the values of the scattered radiations surpass many times those of the primary rays. The practical importance of these facts is very apparent.

Thus far we have considered the dependence of the graph of the dose upon the field size and the relations between the values

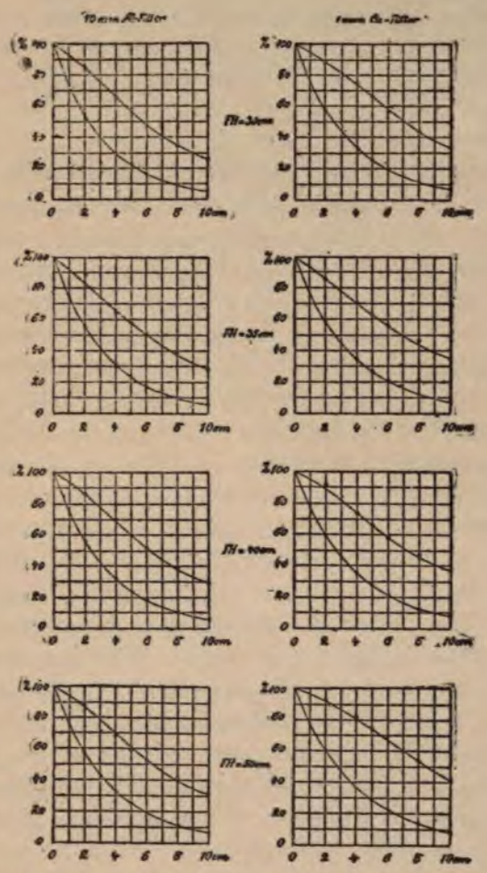


FIG. 68.—Decrease of dose in the deep (measured and calculated values) with filters of 10 mm. Aluminum and 1 mm. Copper. F.H.—30, 35, 40 and 50 cm., port of entry 20 x 20 cm.

of the scattered radiation which had been determined experimentally as well as mathematically. We shall now investigate the dependence of the experimental graphs of the doses on their relation to the calculated graphs with different large F. H. but a constant size of field. We have already determined that the dose in the depth increases with an increasing F. H. in all the field sizes investigated—only slightly in a small field but considerably in a large field. This means that the influence of the law of squares

In all radiations we strike first the skin; in all deep radiations we must penetrate through it. We should not damage the skin but only cause a slight erythema. The question arises how may we develop a technique of radiation based on our physical investigations. The answer to this question cannot be given in one sentence. We may ask what is the purpose of radiations? Is it necessary to bring as high an X-ray dose as possible to a certain depth? Or is it desired to treat diseases of the skin? A proper choice of the factors determining the graph of the doses can only be made after these preliminary questions have been answered.

TABLE 9.

Influence of F.H. on the time of application of a given dose with varying fields of entrance.

| | F. H. | | | | | |
|---|---|---|---|---|---|---|
| Values calculated from the law of squares | 25 cm. 69.5 | 30 cm. 100 | 35 cm. 136 | 40 cm. 177.5 | 45 cm. 225.3 | 50 cm. 278.0 |
| Measured values with 10 mm. Aluminum filter | | | | | | |
| Field size 2 x 2 cm. .... | | 100 | 142.2 | 188.2 | 249.2 | 309.4 |
| Field size 8 x 8 cm. .... | | 100 | 136.2 | 178.0 | 236.0 | 287.3 |
| Field size 14 x 14 cm. .... | | 100 | 139.5 | 186.7 | 255.8 | 329.0 |
| Field size 20 x 20 cm. .... | | 100 | 143.0 | 182.2 | 230.0 | 289.9 |
| Measured values with 1 mm. Copper filter | | | | | | |
| Field size 2 x 2 cm. .... | | 100 | 140.6 | 188.1 | 242.0 | 309.0 |
| Field size 8 x 8 cm. .... | | 100 | 138.2 | 189.0 | 227.3 | 295.0 |
| Field size 14 x 14 cm. .... | | 100 | 135.2 | 173.2 | 226.6 | 294.0 |
| Field size 20 x 20 cm. .... | | 100 | 133.9 | 175.9 | 240.0 | 291.5 |

Let us assume a case in which it is necessary to apply at a great depth (10 cm. beneath the skin surface) as high a dose of X-rays as possible. One will necessarily choose:

1, a very hard ray (1 mm. copper filter),
2, a large port of entry,
3, a large F. H.

It will then be possible to attain the highest deep dose of rays with the highest permissible load to the skin. Since with a large F. H. the decrease of the intensity of the rays from the tube to the region of entry is inversely proportional to the square of the distance, that is, very high, a long time will be required before the desired dose will have been applied. The radiation will be of a long duration and the patient's endurance taxed to the utmost. On the other hand, the use of electric current, the depreciation of the tube and transformer will be very great. The results accomplished relative to all these costs are very small. Since with a large field (20 x 20

cm.) and a decreasing F. H. the quotient of the dose falls rapidly (22.9% with a 10 mm. Al. filter and 27.7% with a 1 mm. Copper filter with a decrease of F. H. from 50 to 25 cm.) it will generally not be possible in this instance to work with a short F. H. The long duration of radiation and the low relative returns must be accepted as necessary evils.

Let us take a second case in which it is necessary to treat a pathologic condition also at a great depth. However, a smaller dose will suffice to attain the necessary results. It will then be possible to attain the desired dose,

1, with the same hardness of rays as in the first case,
2, with the same port of entry, and
3, with the small F. H.

The quotient of the dose will be unfavorable, the skin receiving relatively more rays than in the first case. However, since a much smaller amount of X-rays is required, it will not be necessary to exceed the skin dose. One has then the great advantage of sparing the patient the long exposure and also of operating the instruments on a more economical basis.

If changes in the skin must be treated it is evident that the F. H. should be very short and the hardness of rays correspondingly reduced (decrease of filter), for a heavier filtration arrests the largest part of the rays emitted from the anticathode. Light filters also increase the economy. According to the investigations of Krönig and Friedrich, in which a dosimeter with a graphite measuring chamber was used, it does not matter in so far as the biologic action is concerned whether harder or softer rays are used. A decrease of the F. H. or a decrease of the filter act in the same manner. Whether it is necessary in a certain case to change the one or the other or both of these factors must be decided for each individual case.

The experiments so far described have been performed with an inductor of the Sanitas Company which was operated with a gas interrupter and a Coolidge tube with a storage battery for heating the cathode. To forestall the claim that the results hold good only for this inductor we performed additional experiments with an alternating current instrument—the Intensive-Reform Apparatus of the Veifa Works—which also was operated with a Coolidge tube, and with a Symmetry Apparatus of Reiniger, Gebbert and Schall, with an automatically hardening Müller hot water tube and an automatic Wintz regenerator.

*Experiments with the Intensive-Reform Apparatus Veifa.*

The apparatus was operated with the kilovoltmeter placed at 50 on the scale, which corresponds according to the table to 180,000

volts. The Coolidge tube was charged with a current of 2.5 m. amp., the heating current of the cathode was 3.8 amp. The heating current was not furnished by a storage battery but by a special transformer attached to the apparatus. The decrease of the deep dose was investigated in the water phantom. The series of experiments were performed in exactly the same manner as previously described save that the decrease of the intensity was not determined from 2 to 2 cm., but at 5 and 10 cm. only.

*Experiments with the Symmetry Apparatus—Reiniger, Gebbert and Schall.*

The inductor was operated at a position of 84 to 88 of the scale of the sclerometer corresponding to a parallel spark gap of 35 to 38 cm. The tube was charge with 2.0 to 2.4 m. amp. The measurements were taken in the same manner as with the reform apparatus.

TABLE 10

Deep Doses Measured with Different Transformers

| Depth in cm. | 10 mm. Aluminum Filter Intensive Radiation | Intensive Reform | Symmetry | Depth in cm. | 1 mm. Copper Filter Intensive Radiation | Intensive Reform | Symmetry |
|---|---|---|---|---|---|---|---|
| Size of Field, 8 x 8 cm., F. H. = 35 cm. | | | | | | | |
| 0 | 100.0 | 100.0 | 100.0 | 0 | 100.0 | 100.0 | 100.0 |
| 5 | 50.8 | 50.1 | 50.2 | 5 | 51.4 | 52.0 | 52.3 |
| 10 | 20.9 | 19.6 | 20.2 | 10 | 23.0 | 22.8 | 22.7 |
| Size of Field, 20 x 20 cm., F. H. = 30 cm. | | | | | | | |
| 0 | 100.0 | 100.0 | 100.0 | 0 | 100.0 | 100.0 | 100.0 |
| 5 | 57.8 | 57.4 | 57.2 | 5 | 66.5 | 64.8 | 67.2 |
| 10 | 26.1 | 26.2 | 26.3 | 10 | 33.6 | 34.9 | 34.0 |
| Size of Field, 20 x 20 cm., F. H. = 50 cm. | | | | | | | |
| 0 | 100.0 | 100.0 | 100.0 | 0 | 100.0 | 100.0 | 100.0 |
| 5 | 59.8 | 60.0 | 60.0 | 5 | 73.8 | 74.1 | 73.5 |
| 10 | 31.2 | 31.8 | 30.6 | 8 | 41.4 | 40.6 | 41.0 |

The depth doses measured with the various instruments are given in Table 10. The measurements obtained with the Intensive Reform Apparatus and Coolidge tube and with the Symmetry Apparatus and the Müller hot water tube correspond so closely to those obtained with the Sanitas inductor and Coolidge tube with conditions of operation described, that all criticism is unfounded. It also follows therefrom that the biologic action attained with the different instruments must always be the same, presupposing that the conditions of operation are maintained as described.

The investigations have demonstrated which factors determine the intensity prevailing at a given deep point and how the single factors are dependent on each other. It must therefore be our endeavor in practical therapy to make the measurements at the seat

and region of the disease in each instance if possible. This requirement may be easily fulfilled if the diseased area is located on the surface. It becomes difficult if a deep-seated organ is concerned. However, the latter requirement may also be attained, for instance, in gynecology, by the insertion of the ionization chamber into the vagina or rectum. In other cases this requirement of direct measurement at the seat of the disease is impossible because the seat of the disease is inaccessible or such a measuring chamber is not at hand. We then must confine ourselves to a measurement on the surface and determine from the surface dose the depth dose. To perform a dependable dosation for the depth we must know how and under what conditions the intensity of the X-rays decreases in the depth of the body. It is possible from the course of a graph of a dose with a known hardness of rays, known size of field and known F. H., to follow up and determine the decrease of the dose. It is also possible by interpolation of the values obtained to find those lying between them. It is self-evident on account of the errors attached to such experimental graphs in spite of all precautions, that in the determination of the final values not only a single graph, but the entire series of graphs must be taken into consideration. For instance, the graphs which have been taken with the same hardness of ray, the same field of entrance but varying F. H. In this way we may proceed to construct tables which contain numericals for the decrease of intensity from centimeter to centimeter for a F. H. of 25, 30, 35, 40, 45 and 50 cm., and field sizes of 2 x 2, 8 x 8, 14 x 14 and 20 x 20 cm., and also of the sizes lying between these. (With known surface doses and known location within the body of the diseased area to be radiated, the depth dose can be determined from such tables.)

As such tables would transgress the purpose of this paper and since they are of a special interest for X-ray therapy they have not been presented in this work but will appear in a later paper. Instruments of other manufacture that were not at our disposition for these experiments will also be subjected to investigation. In the meantime we may collectively state:

1. The dose existing at a given point is composed of primary rays and scattered radiation.

2. The graph of the dose runs a straight course:
   (a) the more favorable the quotient of the dose;
   (b) the harder the primary radiation;
   (c) the greater the size of the field, and
   (d) the longer the focus skin distances.

The dependence of the increase of the quotient of the dose upon the F. H. varies with small and large field sizes. The increase with increasing F. H. is only slight with small fields, but considerable with

large fields. In the smaller fields the experimental values approach the values calculated from the law of squares and half absorption value layer.

3. The quantity of rays striking the surface in a unit of time with varying F. H. is in an inverse ratio to the square of distances (F. H.) i.e., the economy of the operation increases quadratically with decreasing values of F. H.

4. With the directions of operation given all the apparatuses examined furnish practically the same quality of radiation. The values obtained experimentally and the tables constructed therefrom have general validity and may serve as a base for a correct dosage in deep roentgen ray therapy.

# EXPERIMENTAL CONTRIBUTION TO THE QUESTION OF SECONDARY RAY THERAPY*

BY W. FRIEDRICH AND M. BENDER

The problem of secondary ray therapy is relatively old. As early as 1910 Albers-Schönberg[1] performed experiments with secondary rays on biologic objects. Hernamann-Johnson introduced finely pulverized silver into the bowels to increase the action of the rays on the diseased part of the bowel by the secondary radiation arising in the silver. Emulsions of bismuth also have been inserted in the body for the same purpose. Other investigators, Steward for example, carried a secondary ray radiator in the solid state in the form of plates, wires and tubes into the tissues to be exposed to the X-rays. Gauss and Lembcke,[2] also Schwarz investigated the influence of the secondary rays from colloidal substances on animal and vegetable cells.

In the monograph written by B. Krönig and W. Friedrich,[3] biologic experiments with solid and colloid secondary radiators have been reported.

The results of the biologic tests and the clinical investigations are not uniform. Some believe to have observed an increase in the biologic action by the secondary radiators, while others could not observe any influence worth mentioning.

From a purely physical and theoretical viewpoint the problem has been quite frequently investigated. G. Grossmann[4] particularly has published a detailed discussion of these questions. In recent times W. Stepp and P. Cermak,[5] influenced by physical considerations, have introduced during clinical radiations colloidal silver in the form of collargol in the bladder and claim to be able to report a positive influence of these secondary radiators. G. Spiess and F. Voltz[6] mention the question of secondary ray therapy in the monograph "Zur kombinierten Chemo- und Strahlentherapie bösartiger Geschwülste" but leave unanswered the question whether the results of the clinical radiations observed could be attributed to the action of colloidal gold as secondary radiator or to a purely chemo-biologic action of this substance.

* Strahlentherapie, Vol. XI, 1920, page 1.

1 Albers-Schönberg, F. d. Röntg. 21, 1914.

2 Gauss u. Lembcke, Röntgentiefenstrahlentherapie, 1912.

3 Krönig-Friedrich, Physik. u. biolog. Grundlagen der Strahlentherapie, 1918.

4 G. Grossman, F. d. Röntg. 22, H. 4.

5 W. Stepp u. P. Cermak, M. med. W. 1918, No. 40.

6 G. Spiess u. F. Voltz, F. d. Röntg. 26, H. 4/5.

The authors mentioned generally entertained the same hypotheses in their investigations.

The object of radiation therapy, particularly of deep therapy is to cause a definite quantity of homogeneous X-rays to be absorbed in the depth of the human body. The quantity of the absorbed radiation energy or the radiation dose must be very large, especially in the treatment of malignant tumors. In the solution of the problem the fact must be considered that the region of the body lying above the disease area to be treated, above all the skin, can receive only a certain radiation dose without suffering damage. To avoid injuries to the skin and yet be able to bring the desired dose to the depth, the rays must be very penetrating. They should be the harder the deeper the diseased focus is located. In other words, the quotient of the dose, i.e., the ratio of the deep dose to the surface dose which is chosen, must be greater the deeper the radiated area is situated, that is, it should approach the value 1.

In spite of the important progress made in the development of transformers or inductors for the production of rays as hard and penetrating as possible, one is oftentimes not in a position, with deeply located diseased areas, to attain the quotient of dose desirable. A special technique of radiation must be used, the so-called cross-fire radiation, to obtain at a designated place and region the desired dose through several ports of entry. Many undesirable side actions result from this method. We only mention the severe damages to the blood which result from the large radiated portion of the body and which may render illusory the treatment. It was natural to hit upon a method of rendering the quotient of dose much more favorable by other means than an increase of hardness of the rays or a further development of the radiation technique. It was thought that this agent had been found in the property of the X-rays by which they excite in certain substances a strong secondary radiation.

We know from the researches of Barkla and his pupils that there are three kinds of secondary rays. The first ray, which has been termed scattered radiation, possesses the same physical properties as the exciting primary ray. It is analogous to the scattering of light rays in an opaque medium. The scattering coefficient is relatively very small. According to Barkla it is only about 0.2 for substances of light atomic weight for all kinds of rays. W. Friedrich[7] has demonstrated that the scattered radiation has an essential importance for the size of the dose, especially with large fields of entry, in spite of the small scattering coefficient. This does not only apply to the use of X-rays but also to the intracorporeal use of the rays of radio-active substances. So far no importance whatsoever has been attributed to this scattered radiation in secondary radiation therapy.

[7] Loc. cit.

We shall see that this view is false and that the scattered radiation plays quite a considerable rôle in secondary radiation therapy.

The second variety of secondary radiation, the so-called secondary characteristic ray or fluorescent ray, is a radiation which does not physically resemble the primary radiation, in contradistinction to the scattered radiation, but is solely and singly characteristic for the substance in which it is excited. Though all substances emit a characteristic ray, only substances of a high atomic weight, such as that of iron or still heavier metals, are of importance for secondary radiation therapy, as only their characteristic radiations can penetrate the surrounding tissues to an appreciable depth. Another point must be considered in this connection, characteristic radiation in media of less atomic weight is not excited to a desirable degree with the hard primary radiation used in present day practice, since the range of the greatest excitation of characteristic radiation has already been surpassed. The ratio of the energy of the characteristic secondary radiation to that of the primary radiation is much higher in contradistinction to that of the scattered radiation. In the most favorable instance about 30 per cent of the absorbed energy is secondarily emitted. On account of the much greater absorption of the primary rays in a secondary radiator of high atomic weight—particularly within the selective range—the absolute amount of the secondary radiation energy is still further increased.

Because of these facts it is obvious that the characteristic secondary radiation of substances of high atomic weight can be used to increase the dose at a given place in the body and thereby the quotient of the dose is improved.

The third variety of secondary radiation, the so-called secondary cathode rays or secondary beta radiation, differs entirely in its physical nature from the two other secondary rays mentioned. It is not an electro-magnetic wave but a corpuscular radiation. As is well known it consists of electrons which move about with a more or less great velocity. The corpuscular nature of this secondary radiation is the reason for the relatively rapid absorption. The beta rays of known high velocity derived from radio-active substances are absorbed in a few millimeters of tissue, while the beta rays excited by the X-rays possess a still smaller penetrability. Though the biologic action of all kinds of rays must finally be attributed to such a beta radiation, its activity is so small that it may be neglected in secondary radiation therapy.

The characteristic secondary radiation therefore is considered to be of importance in secondary radiation therapy. The great influence of the scattered radiation of the radiated tissue on the absolute size of the dose and the dose quotient makes it appear probable that the scattered radiation also plays an important rôle in secondary radiation therapy.

We decided to obtain information on secondary radiation by

experimental researches as the methods of calculation are too complicated. The latter method also does not give exact results as the constants employed therein are not dependable.

We next propounded the question: Are the X-rays used in radiations, especially deep radiation therapy, able to excite secondary rays in a secondary radiator of a kind and amount to render them useful in therapy?

The method of measuring used was the ionization method based on the discharge of a charged electrometer by ionization of the air due to the rays. We employed the same instrument as described on page 10. The ionization chamber was of a disc shape with a volume of 1 ccm. The walls were made of aluminum 0.01 mm. thick. The inner electrode connected to the measuring chamber consisted of a thin aluminum wire. As the ionization chamber was placed within water during the measuring it was rendered watertight by a thin layer of varnish. The walls of the chamber were chosen as thin as possible so that the radiation could enter it in an almost unweakened state.

We paid special care in the arrangement of the apparatus that an undesired secondary radiation could not strike the ionization chamber so that we obtained solely the effect of the secondary radiator.

A Coolidge tube with a tungsten anticathode served as a source of radiation for the X-rays. The tube was contained in a bowl lined with heavy leaded rubber and attached to a stationary stand. A movable diaphragm was placed beneath the tube bowl. The filters also could be inserted at this place in the radiation beam. The tube was operated by a large inductor with gas interrupter. A hot ventil tube was placed in the secondary conductor to avoid a short circuit. The ionization chamber was placed at a distance of 40 cm. from the anticathode in the center of the radiation beam. The rays passed through a fixed opening in the table cover so that only the secondary radiation of the air would appear as undesirable rays during the tests. The intensity of these secondary rays, however, did not have any influence worth mentioning on the result. The secondary radiators to be tested could be placed directly beneath the ionization chamber by means of proper holders.

As it was impossible to examine all the methods of technique and filtration made use of in therapy, we made the following selections: We first employed an X-ray filtered with 3 mm. Al. emitted from a Coolidge tube operated with an inductor and gas interrupter furnishing a voltage with a parallel spark gap of 30 cm. measured between point and disc. Secondly we used an X-ray filtered with 10 mm. Al. arising from a Coolidge tube operated with an inductor and gas interrupter furnishing a voltage with a parallel spark gap of 35 cm. measured between point and disc. The hardest X-ray employed was filtered with 1 mm. copper and was obtained from a Coolidge tube

operated with an inductor and gas interrupter furnishing a current of a voltage having a parallel spark gap of 40 cm. between point and disc.

Secondary radiators of a solid and pulverized state were examined. The second kind was used in the form of aqueous and colloidal solutions.

As solid secondary radiators we chose silver, tungsten, platinum and lead, and for purposes of comparison aluminum. A characteristic secondary radiation was not present within the range of hardnesses maintained in these tests. These materials possessed the form of sheets of different thicknesses. The size was 10 by 10 cm. We had at our disposal only a block of tungsten about 15 mm. thick. The thickness of the sheets sufficed to attain the optimum of action of the secondary radiation. To obtain values of comparison for the tests in the water phantom to be described later on we used the silver and lead in square sheets of a size 15 by 15 cm.

As secondary radiators in a finely divided state we selected the following solutions: Aqueous solutions of potassium iodid of 1 to 40 per cent, barium chlorid of 1 to 14 per cent, sodium wolframat of 1 to about 10 per cent, and finally as a representative of colloidal solutions 1 per cent collargol.

Iodine and silver, in the solutions stated, may be readily inserted in the biologic object, especially the human body; solutions of barium and tungsten cannot be thus introduced. Powdered barium sulphate may be introduced in the stomach and bowels in the form of opaque meals; in this form it is too unhandy for our tests. Other non-poisonous bismuth compounds do exist. The chemical composition does not play any rôle since an even distribution of the secondary radiator is the only requirement necessary for the purely physical problems of secondary radiation.

The solutions were placed in cases of thin celluloid 10 cm. long and wide and 3 cm. high. The sheets of celluloid were less than ½ mm. thick. Hence the secondary rays could reach the ionization chamber in an almost unweakened condition.

The course of the experiment was as follows: The tube was regulated to the desired degree of hardness by adjustment of the hot filament current and the primary current of the inductor. The particular filter was inserted into the ray beam. The tube was run for some time before taking a measurement until it became constant. A measurement was then taken by observing the time during which the electrometer leaf passed through five divisions of the scale, first with the ionization chamber alone in the radiation beam and again when the secondary radiator to be tested had been placed just beneath the ionization chamber. The measurements were repeated several times in order to eliminate fluctuations of the X-ray tube if they were still present. The time values are inversely proportional to the energy which strikes the ionization chamber. The undesired

radiation to be considered and the loss from defects of insulation of the electrometer system were determined by special tests and entered in the final calculation of the results. An extract from the observation journal is given in Table 11. It also serves as an example of the exactness with which the measurements were made. We conclude from these values that the method of measuring is a very exact one.

TABLE 11

Secondary radiator Ag.; X-ray filtered with 10 mm. Al.; Measurement in air, undesired radiation; 142″ for 5 divisions of the scale.

| Time values in seconds of the discharge of the electrometer | | Secondary radiation in per cent of the dose without secondary radiator |
|---|---|---|
| Without Ag. | With Ag. | |
| 29.8 | 24.0 | |
| 29.2 | 24.0 | |
| 29.6 | 23.0 | |
| 29.0 | 24.6 | |
| 28.0 | 24.0 | 17.0% |
| 28.6 | 24.0 | Taking the undesired radiation into consideration: |
| 29.0 | 23.6 | 17.4% |
| 28.6 | 23.6 | |
| 28.6 | 23.6 | |
| 28.0 | 23.0 | |
| Mean value: | Mean value: | |
| 28.8 | 23.7 | |

In Table 12 the results of the measurements in air of the secondary rays of the secondary radiators are given. The different secondary radiators are entered in the first column; the measured values for the secondary radiation in per cent of the dose without secondary radiator are entered in the second to fourth columns for the three varieties of rays used.

Of the solid secondary radiators silver causes the strongest secondary radiations, while the substances of higher atomic weight set up a smaller secondary radiation. In the latter the hardness of the primary rays is evidently not yet sufficient to strongly excite the K-radiation of these substances, while the maximum of the excitation of the essentially softer K-radiation has already been passed.

The results in general show a not inconsiderable secondary radiation and a dependence upon the concentration of the solution is plainly seen. This may be explained by the much more diluted state of the secondary radiator in the soluble form. The secondary rays in this instance can reach the surface from a greater depth in contrast to the solid substances. An appreciable dependence of the intensity of the secondary radiation upon the hardness of the primary ray, within the extent of the hardnesses investigated, is not present. A slight dependence may in general be observed in the sense that the intensity of the secondary radiation is somewhat smaller in the more heavily filtered rays.

TABLE 12

| Secondary radiator | Secondary radiation in per cent. of dose without secondary radiator | | |
|---|---|---|---|
| | Rays filtered with 3 mm Aluminum | Rays filtered with 10 mm Aluminum | Rays filtered with 1 mm Copper |
| Ag 10×10 cm | 17.5 | 17.4 | 17.5 |
| Pb 10×10 cm | 7.1 | 5.9 | 5.2 |
| Pt 10×10 cm | 6.7 | 4.8 | 3.3 |
| Al 10×10 cm 1 mm | 3.5 | 2.6 | 1.8 |
| Al 10×10 cm 5 mm | 3.0 | 2.1 | 0.9 |
| JK 10×10 cm Salt | 17.2 | 16.2 | 13.2 |
| Ba Cl 10×10 cm Salt | 15.7 | 15.7 | 12.9 |
| Ag 2×2 cm | 9.2 | 8.0 | 6.5 |
| W 2×2 cm | 8.2 | 8.1 | 8.1 |
| Pb 2×2 cm | 4.7 | 3.0 | 2.8 |
| JK 1 ‰ | 15.4 | 14.3 | 11.6 |
| JK 1 % | 17.2 | 16.1 | 13.0 |
| JK 10 % | 19.6 | 18.1 | 16.0 |
| JK 20 % | 20.0 | 18.3 | 16.1 |
| JK 40 % | 21.1 | 19.5 | 16.1 |
| $BaCl_2$ 1 ‰ | 12.6 | 11.8 | 9.0 |
| $BaCl_2$ 1 % | 13.6 | 12.7 | 11.1 |
| $BaCl_2$ 10 % | 15.4 | 14.2 | 14.1 |
| $NaWO_4$ 1 ‰ | 13.4 | 12.3 | 10.3 |
| $NaWO_4$ 1 % | 14.1 | 13.0 | 12.2 |
| $NaWO_4$ 10 % | 14.3 | 13.0 | 12.2 |
| Collargol 1 ‰ | 15.9 | 16.2 | 13.4 |

After we had proven by the preceding experiments that a somewhat appreciable secondary radiation is excited in the secondary radiators by the X-rays produced by a definite mode of operation, we approached the solution of the main question:

*Is this secondary radiation able to increase the dose within the biologic object?*

The experimental tests of this question met with very great difficulties in the biologic object. Therefore we used the water phantom described on page 77 since water possesses on the average the same property of absorption of X-rays as the biologic tissue.

The distance from the anticathode to the surface of the water (F. H.) was 40 cm. The size of the field measured on the surface of the water was 15 by 15 cm. With proper supports made of inert material (glass and wood) the secondary radiators could be placed immediately beneath the ionization chamber.

The course of the test closely followed the one described above.

The measurements were performed so that the dosimeter chamber was placed on the surface. The question applied to conditions prevailing in actual practice would be: Is a secondary radiator placed

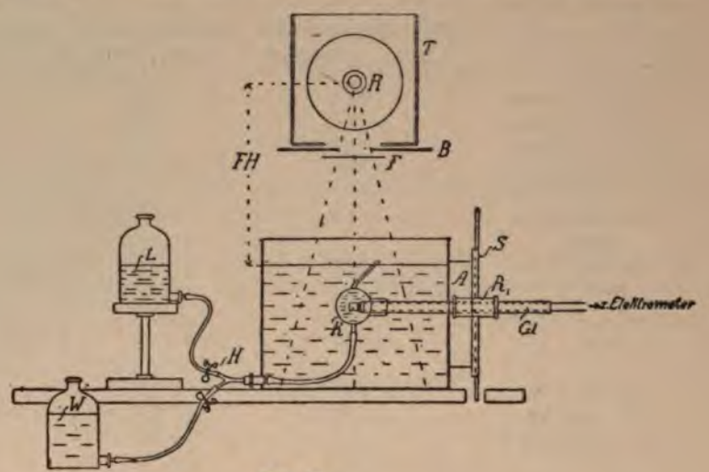



FIG. 69.

close beneath the surface of a biologic object able to increase the dose at the surface? The results of the measurements with the solid secondary radiators are collected in the following table:

TABLE 13

| Secondary radiator | Secondary radiation in per cent. of dose without secondary radiator | | |
|---|---|---|---|
| | Rays filtered with 3 mm Aluminum | Rays filtered with 10 mm Aluminum | Rays filtered with 1 mm Copper |
| Ag | — 5.7 | — 5.7 | — 4.7 |
| Pb | —17.5 | —17.1 | —17.7 |
| Pt | —14.2 | —15.7 | —14.9 |
| Al 1 mm | — 2.5 | — 3.1 | — 2.1 |
| Al 5 mm | — 5.9 | — 5.4 | — 5.1 |

We observe that the dose is not at all increased but is decreased by the insertion of a secondary radiator. This result appears at first to be surprising as we had demonstrated that the hard rays used in our tests are able to excite a relatively strong secondary radiation in these substances. The following consideration will explain the result:

As already mentioned, the scattered radiation of the irradiated region plays an important rôle in the absolute size of the dose. With the field size of 15 x 15 cm. the amount of the dose of the scattered radiation in the tissue in the center of the radiation region is larger than the dose applied directly by the primary rays. A secondary

radiator placed in this tissue area absorbs a part of the scattered rays of the tissue lying beneath the secondary radiator and also excludes them from the area of tissue lying above the secondary radiator. Thereby the absolute amount of the dose is decreased. On the other hand the primary ray forms in the secondary radiator secondary rays that should increase the dose. In this instance the amount of the dose lost by absorption in the secondary radiator is evidently larger than that emitted by the secondary radiator.

The dependence upon the hardness of the primary rays is very slight, if it is at all present.

The conditions are somewhat different if secondary radiators in a finely divided form are employed. Table 14 gives the results of measurements with such substances again taken on the surface of the phantom.

TABLE 14

| | Secondary radiation in per cent. of dose without secondary radiator | | |
|---|---|---|---|
| Secondary radiator | Rays filtered with 3 mm Aluminum | Rays filtered with 10 mm Aluminum | Rays filtered with 1 mm. Copper |
| JK 1 ‰ | +4.6 | +4.1 | +5.9 |
| JK 1 % | +3.8 | +3.0 | +3.1 |
| JK 10 % | +0.4 | +0.4 | +0.2 |
| JK 20 % | —1.2 | —1.1 | —1.8 |
| JK 40 % | —4.1 | —4.7 | —4.1 |
| $BaCl_2$ 1 ‰ | +3.4 | +4.2 | +4.0 |
| $BaCl_2$ 1 % | +1.7 | +2.5 | +3.5 |
| $BaCl_2$ 10 % | —2.2 | —2.8 | —1.8 |
| $NaWO_4$ 1 ‰ | +5.3 | +5.1 | +5.3 |
| $NaWO_4$ 1 % | +2.3 | +3.1 | +3.5 |
| $NaWO_4$ ca. 10 % | —3.0 | —3.7 | —2.7 |
| Collargol 1/00 | +4.1 | +4.6 | +3.6 |

We see indeed that a slight increase of the dose occurs from the secondary radiators if they are dissolved in water. The amount of the dose excited in the secondary radiator is somewhat larger than the one lost by arrest of the scattered radiation. Here also a dependence of the intensity of the scattered radiation upon the concentration of the solution is shown the same as in the investigations in air. To obtain an instructive picture of these facts the values for solutions of potassium iodid have been entered in the form of graphs in Fig. 70. The values above 1 per cent of the abscissa have been entered in a different scale. The lower curve refers to the values of the dose in the depth.

We deduce from the course of the graphs that weak solutions of the secondary radiators cause an increase in the dose. With solutions of about 18 per cent the secondary radiation dose and the dose lost through absorption of scattered rays are in equilibrium. We obtain the same value of dose as if a secondary radiator had not at

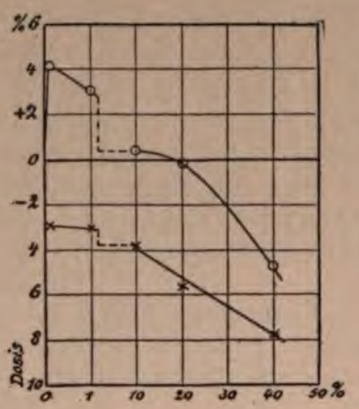



FIG. 70.—Dependence of the secondary radiation on the concentration of the solution in per cent. of the dose without secondary radiator.

all been used. With higher concentrations the values are again negative, due to the strong filtration and consequent absorption. This observation may again be attributed to concentration of the solution of the secondary radiators.

Following these experiments we next conducted the tests in the deep regions of the phantom. We raised the following question: Are the secondary radiators able to increase the dose in the biologic object at a depth of 5 cm.?

The results of the measurements are collected in the following table for solid as well as for finely divided secondary radiators.

TABLE 15

| Secondary Radiator | Secondary radiation in per cent. of the dose without secondary radiator: X-rays filtered with 3 mm Aluminum | X-rays filtered with 10 mm Aluminum | X-rays filtered with 1 mm Copper |
|---|---|---|---|
| Ag | — 4.2 | — 4.0 | — 4.2 |
| Pb | —14.4 | —16.2 | —14.0 |
| Pt | —13.1 | —14.1 | —13.1 |
| Al 1 mm | — 1.3 | — 1.1 | — 1.6 |
| Al 5 mm | — 3.7 | — 4.1 | — 5.2 |
| KI 0.1% | — 2.2 | — 2.9 | — 1.3 |
| KI 1% | — 2.7 | — 3.1 | — 2.3 |
| KI 10% | — 3.8 | — 3.8 | — 2.2 |
| KI 20% | — 5.9 | — 5.6 | — 6.1 |
| KI 40% | — 7.6 | — 7.7 | — 6.7 |
| $BaCl_2$ 0.1% | — 2.1 | — 1.7 | — 1.5 |
| $BaCl_2$ 1% | — 2.8 | — 1.8 | — 1.7 |
| $BaCl_2$ 10% | — 6.3 | — 5.4 | — 4.4 |
| $NaWO_4$ 0.1% | + 1.1 | + 1.4 | + 1.9 |
| $NaWO_4$ 1% | — 2.9 | — 2.6 | — 2.8 |
| $NaWO_4$ 10% | — 6.6 | — 5.9 | — 4.7 |
| Collargol 0.1% | — 2.4 | — 2.1 | — 2.3 |

We deduce from these values that the dose is diminished by the solid secondary radiator in the same degree as on the surface. The values obtained using secondary radiators in finely divided form are also negative with the exception of those obtained with the 1 per cent solution of sodium tungstenate, in which case values on the surface also were relatively the greatest. With tungsten a rôle may be played by the fact that it absorbs its own characteristic radiation in less degree; it is therefore more permeable for its own char-

acteristic radiation. The characteristic radiation of tungsten as a pronounced component is indeed present in the primary rays as a K-radiation on account of the tungsten cathode of the X-ray tube and the voltage used. This has been verified by spectroscopic examination. The generally much smaller values of the dose in comparison to those found on the surface may be explained by the fact that the primary radiation becomes increasingly hardened by passing through the layer of water above the dosimeter chamber. The excitation of the soft L-radiation of the heavy elements, as the relatively soft K-radiation of the elements Ag, I and Ba, will be less pronounced at the surface, because the mean hardness of the primary rays has been removed farther from the range of greatest excitation. The hard K-radiation has probably not as yet been sufficiently excited in the heavier metals. If a Roentgen tube with platinum anticathode, for instance a Lilienfeld tube, is used, in the spectrograph of which the K-radiation of Pt. appears as the strongest component with the method of operation and filtration employed, the K-radiation of tungsten is not excited in a sufficiently marked manner. This was verified by several tests. It might perhaps be possible by using still harder primary radiations obtained by increasing the potential at the tube to excite the K-radiation of the heavy metals as tungsten, platinum, and so forth, to the point that the K-radiation may gain a still greater importance for secondary radiation therapy.

A dependence of the dose upon the concentration of the solution is again present in the same degree and behavior as previously stated. The lower graph in Fig. 70 represents the values of potassium iodid.

The arrest of the scattered rays of the irradiated region by the secondary radiator in the biologic tissues explains the decrease of the dose in the tissue lying above the secondary radiator. If this hypothesis is correct we must deduce that the size of the field possesses an influence on the results of measurements.

The amount of the total dosage which the tissue received in the center of the radiation field from the scattered rays of the irradiated tissue is obviously dependent on the field size, as has been shown previously. The use of the same sized secondary radiator will the more arrest the scattered radiations from the tissues lying above it the larger the field size is, while the amount of the dose of the secondary rays excited in the secondary radiator which strikes the tissue areas remains the same. In small radiation fields the action of the secondary radiator must be more intense than in the larger fields.

In the following tables the results of our investigations with varying field sizes of 2 to 15 cm. square have been compiled. The secondary radiators used were silver, lead and tungsten in the form of sheets of 2 cm. square. The details and method of measurement were the same as in the former tests.

TABLE 16

Dependance of the dose from the size of field (secondary radiator just beneath the surface)

| Secondary radiator | Secondary radiation in per cent. of dose without secondary radiator and a field size of | | | | | Hardness of rays |
|---|---|---|---|---|---|---|
| | 2×2 cm | 4×4 cm | 6×6 cm | 8×8 cm | 15×15 cm | |
| Ag | +3.2 | +1.2 | —3.3 | —3.8 | — 4.6 | Rays filtered |
| W | +2.3 | —2.2 | —3.5 | —5.1 | — 8.1 | with 3 mm Al. |
| Pb | —3.5 | —3.8 | —4.3 | —5.9 | — 8.2 | |
| Ag | +3.4 | +0.7 | —3.5 | —3.7 | — 4.9 | Rays filtered |
| W | +3.4 | —3.0 | —3.1 | —4.1 | — 7.4 | with 10 mm Al. |
| Pb | —2.3 | —4.2 | —5.5 | —6.2 | — 8.7 | |
| Ag | +3.1 | +1.2 | —2.6 | —3.5 | — 4.3 | Rays filtered |
| W | +3.1 | —2.8 | —4.2 | —4.8 | — 7.0 | with 1 mm Copper |
| Pb | —2.4 | —4.7 | —4.4 | —7.3 | — 9.2 | |

TABLE 17

Dependance of the dose from the size of field (secondary radiator in a depth of 5 cm)

| Secondary radiator | Secondary radiation in per cent. of dose without secondary radiator and a field size of | | | | | Hardness of rays |
|---|---|---|---|---|---|---|
| | 2×2 cm | 4×4 cm | 6×6 cm | 8×8 cm | 15×15 cm | |
| Ag | +4.2 | +1.3 | —2.5 | —3.5 | — 5.4 | Rays filtered |
| W | +3.2 | —3.2 | —5.9 | —8.2 | —10.8 | with 3 mm Al. |
| Pb | —1.1 | —4.1 | —5.8 | —6.7 | —11.3 | |
| Ag | +4.1 | +1.4 | —2.6 | —4.8 | — 5.1 | Rays filtered |
| W | +3.6 | —2.9 | —5.1 | —6.4 | —10.3 | with 10 mm Al. |
| Pb | —0.9 | —4.0 | —6.1 | —8.2 | —10.2 | |
| Ag | +4.1 | +1.2 | —2.4 | —3.9 | — 5.1 | Rays filtered |
| W | +3.1 | —3.1 | —5.1 | —6.1 | —11.5 | with 1 mm Copper |
| Pb | —1.6 | —3.5 | —5.9 | —6.0 | —11.3 | |

As a matter of fact we see that the suspected dependence is present at the surface and at a depth of 5 cm. Figs. 71 and 72 represent the values in the graphs for silver and tungsten at the surface.

In the preceding paragraphs we investigated the influence of the secondary radiator on the dose in such a way that the solid or finely divided secondary radiator was placed beneath the dosimeter chamber, therefore beneath the tissue area to be radiated. This method of application of the solid secondary radiation is the only one of practical importance, while that of the finely pulverized or dissolved secondary radiators is in most instances different. The dissolved secondary radiator is distributed over the whole region to be exposed to the X-rays, for instance by injecting solutions of potassium iodid into the tumor. We therefore raise the question: Has the presence of a secondary radiator in aqueous solution distributed within the tissue area to be treated an influence on the size of the dose within this area, for instance on the size of the dose which a tissue area receives in the center?

To subject the question to an experimental solution we employed a kind of tumor phantom. We surrounded the ionization chamber with a hollow glass ball of a diameter of an average sized tumor, i. e., 6 cm. Two glass tubes were attached to the walls of the glass ball at opposite points. The lower one served for the introduction of the

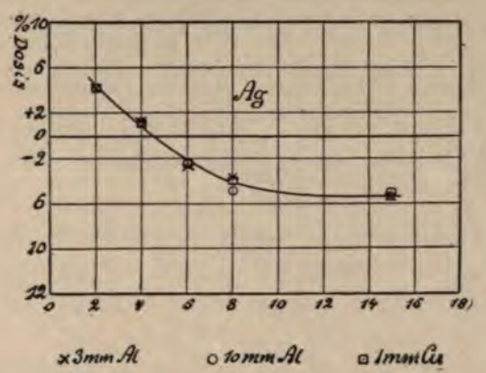



FIG. 71

secondary radiator in liquid form or of plain water, if it was desired to remove the secondary radiator. The upper tube served for the escape of air from the glass ball. The outlets were connected by rubber tubes with the glass bottles L and W, which contained either

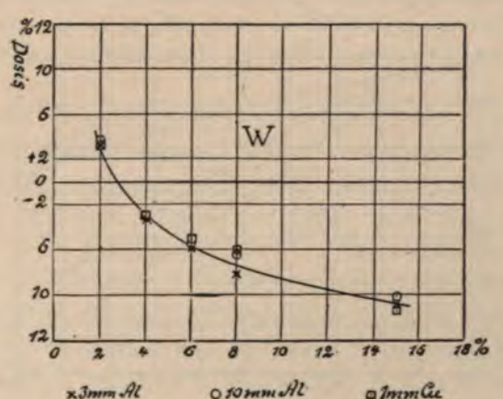



FIG. 72.—Dependence of the secondary radiation on the size of field in per cent. of the dose without secondary radiator.

the solution of the secondary radiator or water. See Fig. 69. Through the stopcocks H and by lowering or raising the respective bottles the glass cavity could be quickly filled with the desired liquid. The measurement was performed so that the glass ball was successively filled with water or with the secondary radiator. The dose

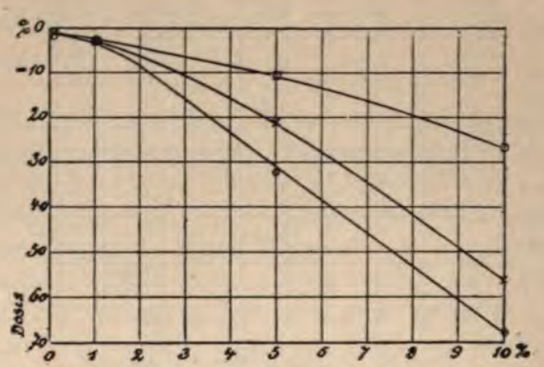
was always determined with a constant primary radiation. Otherwise the course of the experiment was the same as previously observed.

The results of these tests are shown in the following table:

TABLE 18.

| Secondary radiator | Secondary radiation in per cent of dose without secondary radiator | | |
|---|---|---|---|
| | Rays filtered with 3 mm Aluminum | Rays filtered with 10 mm Aluminum | Rays filtered with 1 mm Copper |
| JK 1 ‰ | — 1.8 | — 1.1 | — 1.5 |
| JK 1 % | — 2.5 | — 2.9 | — 2.7 |
| JK 5 % | —32.2 | —21.1 | —10.3 |
| JK 10 % | —67.9 | —56.0 | —26.4 |
| $BaCl_2$ 1 ‰ | — 0.4 | — 0.4 | — 0.8 |
| $BaCl_2$ 1 % | — 2.8 | — 2.6 | — 2.3 |
| $NaWO_4$ 1 ‰ | + 2.5 | + 1.8 | + 2.3 |
| $NaWO_4$ 1 % | — 1.1 | — 0.3 | — 0.3 |
| Collargol 0.5 ‰ | + 0.1 | + 1.2 | + 1.3 |
| Collargol 1 ‰ | — 1.2 | — 0.9 | — 0.7 |

Perusing these values we observe that on an average a somewhat more favorable total dose is obtained with the weaker solutions than with the use of the solid secondary radiators in the deeper tissues beneath the diseased area. An increase of the dose through the




□=3 mm. Al.; ×=10 mm. Al.; o=1 mm. Copper

FIG. 73.—Influence of the concentration of the solution of the secondary radiator KI on the dose.

secondary radiator is here also present only in the case of $NaWO_4$ solution, due to the same reasons previously cited. The values drop quite perceptibly with the stronger solutions, as in the case of 10% KI solution down to 32%. The absorption of rays in the solution

above the dosimeter chamber plays here an important rôle. The dose of the primary rays directly applied to the region of the measuring chamber is greater in less concentrated solutions than in the concentrated forms. On the other hand a larger per cent of secondary radiation and also scattered radiation reaches the dosimeter chamber on account of the more even distribution of the secondary radiator. Fig. 73 shows the values of KI in a graphic presentation.

Reviewing the investigations collectively we may summarize:

1. A rather pronounced secondary characteristic radiation is excited in the secondary radiators within the range of hardness of the X-ray employed.

2. In the biologic object or water phantom the influence of the secondary radiator on the dose, in the sense of an increase, is slight when applied, as shown in these tests. A diminution in the dose occurs in most of the cases through absorption in the secondary radiator of the scattered rays of the tissue area beneath the secondary radiator.

3. The action of the soluble secondary radiators depends on the degree of concentration of the solution. It is greatest in a positive sense with the relatively weak solutions.

4. The size of the radiation field is of influence on the action of the secondary radiator. The action is more marked in small fields than in the larger ones.

5. Secondary radiation therapy is therefore of doubtful merit in therapy with the hardnesses of rays at present at our command.

The method of the dosimeter procedure which is based on ionization, permits the measurement of rays entering the ionization chamber that are of the character of X-rays. The beta rays emitted from the secondary radiator cannot penetrate into the interior of the ionization chamber to ionize the air in the chamber even through very thin walls. Though in radiation therapy a great deal of importance has so far not been attributed to the beta radiation because it is very readily absorbed, still we know that a hard beta radiation appears within the range of selective absorption when we use secondary radiators of high atomic weight. The biologic action of the X-rays is certainly an indirect one and due to the action of the beta radiation excited. The action of beta rays is confined to relatively very small areas on account of their great absorbability in tissue. The cells surrounding the individual molecules of the liquid secondary radiator or the granules of molecules of the colloidal radiators are exposed to a hard beta radiation.

We therefore cannot overlook the possibility that an increase of the general action of the total radiation may take place in the denser

tissue layers if a strong beta radiator is present in a finely divided state. If a solid secondary radiator is used a thin layer of tissue lying adjacent to the radiator is struck by the beta rays. The experimental investigation of the influence of the beta rays of a secondary radiator on the dose by the ionization method of measurement is not possible because the beta-rays cannot enter the measuring chamber.

# THE DISTRIBUTION OF THE RADIATION DOSE IN INTRACORPOREAL RADIUM AND MESOTHORIUM THERAPY*

BY W. FRIEDRICH AND OTTO GLASSER

The intracorporeal radiation treatment of benign and malignant tumors, for instance of the body or cervix of the uterus, has shown that the action of the rays on the diseased tissues is less favorable the farther the tissue is removed from the source of radiation. The explanation is that the dose of the rays which is applied during a known time duration of irradiation is smaller the greater the distance of the tissues from the source of the radiation. The decrease of the dose with the increase in distance is due to the dispersion and the absorption of the rays in the tissue area traversed. The influence of the dispersion on the intensity of the dose is determined by the laws of squares. The degree of the absorption of the gamma-rays of radium or of mesothorium is also known through the investigations of Mayer and Keetmann, although the results of the measurements of absorption by these investigators differ due to the difference in the details of the methods of measurement of the absorption employed.

The decrease in the dose with increase in distance from the source of radiation is not of any import in the treatment of small surface tumors as skin cancers. However it is of great importance in the treatment of larger tumors and especially of deeply situated internal tumors. Experience has taught us that in the latter instances the diseased tissue is not the only one damaged by the rays, but the normal tissue lying within the range of the radiation field is also damaged, though to a lesser degree. If the diseased tissue to be radiated is located more distantly from the source of rays than the normal tissue it has been frequently observed that the healthy tissue may evince a severe reaction though the abnormal tissue has not been acted on to the degree desired. Such conditions may prevail in cancers of the uterus, the cervix, and of the rectal or the vesical mucosæ.

It is evident that attempts have been made to obtain an accurate knowledge of the exact action of radium or mesothorium existing in the immediate surroundings of the radio-active capsule inserted

* Strahlentherapie, Vol. XI, 1920, page 20.

within the body cavities. In 1914 B. Kroenig and J. Koenigsberger[1] propounded a formula for the intensity of rays for the purpose of calculating the distribution of the dose. It is written $1 = \frac{m}{d^2}(1-a)^d$. 1 means the intensity of the impulse obtained at a given location where the dose is to be determined; m the activity of the capsule in milligrams of radium bromid; d the distance of the capsule from the region of the body to be rayed; a indicates the energy absorbed in one cubic centimeter of tissue, which, of course, is always a fraction of the energy originally emitted. E. v. Seuffert[2] proposed a similar calculation in which besides the two factors mentioned in the previous formula, another factor was added, namely, the geometrical form of the radiation capsule. Recently E. Kehser,[3, 4] published articles on the deep action and the stimulation dose of radium and mesothorium. He uses the same formula as Kroenig and Koenigsberger for the calculation of the dose from the laws of distance and absorption, however with the difference that he calculates with radium element instead of radium bromide. He enters into a lengthy discussion on the distribution of gamma radiation in human tissue, on the cancer dose, on the melting dose of cancer tissue, on the stimulation dose of malignant epithelial cell tumors, and so forth. Calculations of the radiation dose have been published by Adler,[5] who took the geometrical size and form of the radium capsule into consideration with the result that the tubular form of radio-active preparations causes a much greater decrease in the dose with distance than would appear from the law of squares or the inverse ratio.

We intend to discuss the purely physical aspect of the distribution of the intensity of the dose and will not touch on the biologic significance. The purpose of this investigation is to demonstrate that the methods, used hitherto, to calculate the dose solely from the laws of distance and absorption lead to faulty results. A very important factor, namely the secondary radiation arising in the radiated structures and tissues, has not been considered. The geometrical form of the radio-active capsule has also not been sufficiently evaluated in the publications mentioned.

The investigations made on the distribution of the dose of X-rays have been extended to that of radium and mesothorium. Although the experimental investigations of all the factors to be considered in this section, for instance filtration, have not as yet been concluded, we deemed it advisable to communicate the results of the measure-

[1] B. Kroenig und J. Koenigsberger, Dt. med. W. 1914, No. 15/16.

[2] E. v. Seuffert, Experimentelle und klin. Untersuchungen usw., Urban & Schwarzenberg, 1917.

[3] E. Kehrer, M. med. W. 1918, No. 27.

[4] E. Kehrer, Die wissenschaftlichen Grundlagen und Richtlinien der Radiumbehandlung des Uteruskarzinoms. F. f. Gyn. 108, H. 2 und 3.

[5] L. Adler, Die Radiumbehandlung maligner Tumoren in der Gynäkologie. 4. Sonderband der Strahlentherapie. Urban & Schwarzenberg, Berlin, 1919.

ment of the distribution of the dose on account of the great urgency and importance of the matter.

The method of measuring employed in these investigations adheres closely to that described in the distribution of the X-ray dose. Preliminary experiments had shown that water possesses the same properties of absorption of gamma-rays in the mean as the average human tissue. Therefore water was also used in these experiments with gamma-rays.

The method of measuring the distribution of the dose was the ionization method. The ionization chamber was built as small as possible and could be inserted into the phantom like a probe into a body cavity. Therefore the dose could be measured at any point desired within the radiated water. The details are described in the following paragraph. Fig. 74 is a schematic reproduction.

Tr. is a glass vessel 40 cm. long, 30 cm. high and 30 cm. wide. The ionization chamber K was placed in the center of the vessel. The wall of the ionization chamber was made of aluminum sheeting 0.2 mm. thick. The electrode also consisted of a thin aluminum rod. The use of aluminum in the construction of the chamber does not harbor any sources of error if the hardness of the rays to be meas-

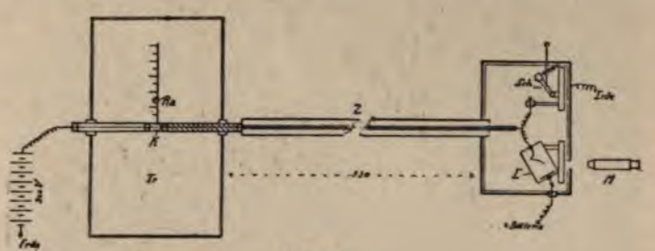


FIG. 74.

ured remains approximately the same. The air volume of the chamber was 0.5 ccm. Two conductors were attached to the ionization chamber. They were well insulated with amber and paraffin and tightly fixed in the walls of the glass vessel with hard rubber plugs. One of the conductors was connected to a storage battery of a potential of 200 volts and served to charge the electrical field necessary for the production of the saturation current in the ionization chamber. The other conductor, 2.50 meters long, formed the connection between the inner electrode of the ionization chamber and the electrometer E. We used a Wilson electrometer. The position of the gold leaf could be determined with the reading microscope M which was provided with a scale in the occular. Thus the electrical tension in the electrometer could be measured. The switch Sch served to ground the electrometer system. It was enclosed in a metal case which was grounded to avoid electrostatic disturbances. The imbedding of the conductors in paraffin, the employment of a heavy sheet iron case lined with pasteboard to enclose the electrometer and

the grounding device served the purpose of reducing to a minimum any undesirable radiation and ionization in the conductors and the electrometer. The radio-active preparation Ra was attached to a holder made of thin aluminum, which could be placed at any desired distance in relation to the ionization chamber. A scale of celluloid permitted to measure the distance of the capsule from the ionization chamber. The glass vessel was filled with water during the experiments for the determination of the distribution of the dose in the intracorporeal applications of radio-active substances. Thus the ionization chamber was surrounded on all sides with a layer of water 10 cm. thick. Fig. 75 represents a photographic reproduction of the measuring apparatus.

The measurements were taken so that the time was observed in which the electrometer leaf showed an excursion equal to four divisions of the scale by ionization of the air in the chamber. Starting with a position of the ionization chamber at a distance of 1 cm.

FIG. 75.

from the longitudinal center of the capsule, the latter was always moved one or two centimeters farther from the chamber and the time determined for the excursion of the leaf through four divisions of the scale. After each measurement, for the purpose of control, a reading was made with the radium capsule in the starting position. The time periods consumed are inversely proportional to the dose which a volume of tissue or substance corresponding to that of the ionization chamber absorbs within the same period of time.

As sources of errors cannot be avoided with the use of electrostatic methods, especially in the measurement of gamma-rays of radium

and mesothorium, they were determined by preliminary tests and entered in the final values.

The most important sources of errors are:

1. *The Undesired Radiation.*—The deflection of the electrometer leaf does not solely depend on the direct radiation which enters the ionization chamber. An undesired radiation is added by ionization of the air spaces in the paraffin of the conductor and the air in the electrometer case. To render this undesired radiation as small as possible special care was taken that the paraffin filled the conducting tubes as completely as possible to obviate any small air spaces and that the electrometer was placed at a relatively great distance from the radio-active preparation. Comparing the proportionately large air volume of the electrometer with the minute air volume of the ionization chamber it is evident that the undesired radiation is quite considerable in spite of the great distance of the electrometer from the radiation source. As the time within which an excursion through four divisions of the scale is measured appears too small, due to the action of the undesired radiation, the time must be proportionately increased in the final correction.

2. *Insulation.*—Another source of error is found in a defective insulation of the electrometer system. The insulation of our instrument was of a dependable quality, as amber and purified paraffin were used as insulation materials. A glass disc filled with concentrated sulfuric acid was placed in the case of the electrometer to remove all moisture. Defective insulation causes an increase in the time duration within which a dose is measured, as part of the charge when it travels to the electrometer is always lost by a defect in the insulation. The time measured must be correspondingly reduced in the final correction.

3. *Errors of the Dielectric.*—The dielectric error is intimately connected with the insulation error. Part of the electric charge creeps into the dielectric during the charging of the system, to leak out during the grounding. If one starts the measurements with the unpolarized state of the dielectric, too long a time for the dose will be measured the same as if part of the charge had become lost by a defective insulation. The time measured must be reduced by a proper correction. However if a measurement is taken shortly after the dielectric has become polarized the reverse will take place. By experiments it was demonstrated that the error of the dielectric in the measurements may be reduced to a negligible size if long intermissions are inserted between the individual measurements. Errors of the insulation and the dielectric influence the behavior of the electrometer in a manner directly opposite to that of the undesired radiation. The experiments showed that the undesired radiation does not only equal but surpass the loss caused by defective insulation and dielectric. A subtraction or addition in time due to the

errors was made before and after each series of measurements and considered in the final determination of the dose.

4. Finally the error must be mentioned arising from an incorrect reading of the microscope and from an inexact adjustment of the distance to be maintained between the radium capsule and the ionization chamber. These, however, may be neglected. Proper exactness and carefulness in adjustment and reading should prevent such errors.

TABLE 19.

| Distance in cm. | Measured dose in per cent of dose at distance of 1 cm. | Dose in per cent of dose at distance of 1 cm, calculated from laws of distance and absorption | Difference in per cent of calculated dose. |
|---|---|---|---|
| 1 | 100. | 100. | 0. |
| 2 | 23.2 | 22.5 | 3.1 |
| 3 | 10.4 | 9.0 | 15.6 |
| 4 | 5.4 | 4.55 | 18.7 |
| 5 | 3.3 | 2.62 | 25.9 |
| 6 | 2.2 | 1.64 | 34.1 |
| 8 | 1.2 | 0.72 | 66.6 |
| 10 | 0.7 | 0.39 | 79.5 |

The results of a few tests are reproduced in Table 19. They were made with a mesothorium capsule of a radio-activity of 46.46 mg. radium element. It was enclosed in a silver capsular container 2.28 cm. long and of a diameter of 0.46 cm. This was inserted into a filter capsule made of brass of a wall thickness of 1.5 mm. to arrest the primary beta radiation. In the first column the distances of the ionization chamber from the preparation are entered; in the second the values of the dose in per cent of the dose measured at a distance of 1 cm. from the radio-active preparation which was placed at 100; the third contains the dose calculated from the laws of distance and absorption also in per cent of the dose at a distance of 1 cm. In the last column the difference in the measured and calculated doses is entered in per cent of the calculated dose.

We see from the table that the secondary radiation arising in the radiated tissue or water by the action of radium or mesothorium during its application possesses a remarkable influence on the size and distribution of the dose. The portion due to secondary radiation in comparison to that due to the primary radiation is the larger the greater the distance from the radium capsule grows. The latter is commonly known as the focus skin distance in X-ray therapy. In this instance of intracorporeal application the ratio increases from 0.5 to 79.5% of the calculated dose.

To prove that in these tests the secondary rays arising in the radiated area of the water cause the difference in the measured and calculated doses, we add in Table 20 the results of an experiment in which the decrease of the dose with increase in distance of the cap-

sule from the ionization chamber was measured in the empty phantom. This table also serves as an illustration of the method of reading the values and of correcting the error due to undesired radiation, defective insulation and dielectric, in the final values of measurement.

TABLE 20.

Undesired radiation before measurement: 25 mm. for 4 divisions of scale
Undesired radiation after measurement: 24 mm. for 4 divisions of scale

| Distance in cm. | 4 divisions of scale of electrometer in seconds. | Added values of undesired radiation in seconds | Corrected values | Measured dose in per cent of dose at distance of 1 cm. | Calculated dose in per cent of dose at 1 cm. distance. |
|---|---|---|---|---|---|
| 1 | 17 | 0.05 | 17.2 | | |
| 2 | 66 | 0.18 | 69 | 100. | 100. |
| 1 | 17 | | 17.2 | | |
| 3 | 140 | 0.37 | 154 | 25. | 25. |
| 1 | 17 | | 17.2 | | |
| 4 | 240 | 0.64 | 286 | 11.2 | 11.1 |
| 1 | 17 | | 17.2 | | |
| 5 | 335 | 0.90 | 433 | 6.0 | 6.3 |
| 1 | 17.2 | 0.05 | 17.4 | 4.0 | 4.0 |
| 6 | 466 | 1.24 | 676 | 2.6 | 2.8 |
| 1 | 17.2 | | 17.4 | | |
| 8 | 676 | 1.80 | 1229 | 1.4 | 1.5 |
| 1 | 17.2 | | 17.4 | | |
| 10 | 793 | 2.1 | 1669 | 1.0 | 1.0 |

Columns 1, 5 and 6 have the same measuring as columns 1, 2 and 3 of Table 19. The values in column 6 were obtained by calculation according to the law of squares. Column 2 contains the time values in seconds within which the electrometer leaf passed through four divisions of the scale. Column 3 shows the values of the undesired radiation, while column 4 presents the final values with the corrections based on the sources of errors.

The minute secondary radiation and the slight absorption of gamma-rays in the air are of such small importance that the measured values conform closely to the values calculated from the law of distance.

In medical practice, especially in the treatment of carcinomata of the uterine body, it is often necessary to use several preparations of radium or mesothorium to increase the length of the radiation field to such an extent that it conforms to the size of the growth. The increase in the length of the radium carrier causes a further difference in the actual values of the distribution of the dose from those calculated according to the formula given in a preceding paragraph and based on distance and absorption. This difference in the calculation from the measured values is dependent on the influence of the secondary radiation and on the fact that the source of radiation has always been assumed to be a point or spherical body. The influence of the geometrical form of the radio-active capsule on the values of intensity may be calculated. However, it appears to be much more

exact to determine it experimentally. We employed for this purpose three capsules of mesothorium each of about the same length and strength. They had approximately the size of the capsule described above. The three capsules were placed in a brass capsule of a thickness of 1.5 mm. and a length of 8.28 cm. The measurements were executed in the same manner as previously described. The decrease of the dose with the increase in distance from the radiation source was determined in the center of the longitudinal axis of the applicator. The measurements were first made in the empty phantom. The results are shown in Table 21. The interpretation of the table is the same as that of Table 20.

TABLE 21.

| Distance in cm. | Measured dose in per cent of dose at distance of 1 cm. | Calculated dose in per cent of dose at distance of 1 cm. | Difference in per cent of the calculated dose. |
|---|---|---|---|
| 1 | 100. | 100. | 0. |
| 2 | 30.5 | 25.0 | 22.0 |
| 3 | 15.0 | 11.1 | 34.9 |
| 4 | 9.3 | 6.3 | 48.8 |
| 5 | 6.3 | 4.0 | 57.6 |
| 6 | 4.6 | 2.8 | 67.0 |
| 8 | 2.6 | 1.5 | 66.5 |
| 10 | 1.6 | 1.0 | 60.0 |

From the table it is seen that a considerable difference exists between the measured and calculated values. The latter were obtained from the laws of squares assuming that the source of radiation is of a spherical form.

The secondary radiation emitted from the radiated tissues, in this instance the water, must be added to these values when such extensive and strong preparations are employed in treatment. The distribution of the dose from such long applicators is depicted in the following table.

TABLE 22.

| Distance in cm. | Measured close in per cent of dose at distance of 1 cm. | Dose calculated from the laws of squares and absorption in per cent of dose at distance of 1 cm. | Difference in per cent of calculated dose. |
|---|---|---|---|
| 1 | 100 | 100 | 0 |
| 2 | 32.4 | 22.5 | 44.0 |
| 3 | 15.7 | 9.0 | 74.5 |
| 4 | 9.3 | 4.55 | 104.5 |
| 5 | 5.6 | 2.62 | 113.5 |
| 6 | 4.2 | 1.64 | 156.0 |
| 8 | 2.4 | 0.72 | 233.5 |
| 10 | 1.5 | 0.39 | 285.0 |

It is shown that even more considerable differences between the measured and calculated doses exist than seen in Table 20. At a distance of 5 cm. from the center of the radiation source the difference is 113.5 per cent of the calculated dose.

To render a graphical presentation of the distribution of the dose in radiated tissue one proceeded with the conception that the equal intensity curves of like doses in a body, which we may term "isodoses," are spheres which surround the center of the preparation concentrically. Adler has considered the form of the radiation source in so far as he assumed the isodoses to be of a cylindrical form with semicircular ends, the curves surrounding the capsule parallel to its surface. From a theoretical consideration or viewpoint this should be correct. However, the isodoses of such strong capsules as are used in deep therapy must deviate from the circular or cylindrical forms, for the influence of the size and form on absorption differs accordingly whether one starts the measuring from the center or from another point of the source of radiation. The absorption of the high atomic radio-active salts in the direction of the longitudinal axis must be of special significance for the course of the equal intensity curves.

We, therefore, measured the decrease of the dose with distance at differently located points for the small and large radio-active capsules. Besides the determination of the intensity in the direction vertical to the center of the longitudinal axis, we also performed them at the ends vertically to, as well as in the direction of the longitudinal axis. The results of these measurements with the small capsule are given in Table 23.

The second column gives the doses vertically to the center of the longitudinal axis in per cent of the dose at a distance of 1 cm. In the third column the corresponding values are entered measured vertically to the end of the longitudinal axis also in per cent of the dose in the center of the capsule at a distance of 1 cm. The last column contains the values of the dose in the direction of the longitudinal axis again in per cent of the dose at a distance of 1 cm. in the center of the longitudinal axis.

We conclude from the table that the decrease of the dose with distance at the end of the capsule, vertically to, and in the direction

TABLE 23.

| Distance in cm. | Dose measured in center | Dose measured at end vertical to longitudinal axis | Dose measured at end in direction of longitudinal axis |
|---|---|---|---|
| 1 | 100. | 70.0 | 25.0 |
| 2 | 23.2 | 20.0 | 9.4 |
| 3 | 10.4 | 9.0 | 5.0 |
| 4 | 5.4 | 5.0 | 3.2 |
| 5 | 3.3 | 3.1 | 2.1 |
| 6 | 2.2 | 1.9 | 1.4 |
| 8 | 1.2 | 0.9 | 0.8 |
| 10 | 0.7 | 0.5 | 0.5 |

of the longitudinal axis, differs from that measured in the center. The decrease at the ends is a more gradual one. Fig. 77 represents the values of the tables in graphs.

The results obtained with one capsule permit the conclusion that the deviations must be still more pronounced with the more extensive radiation source. Besides the intensities already determined with the large radium carrier, the decrease of the dose at a point midway between the center and the end was obtained. The results of all the measurements of the large carrier are given in the following table. All values are expressed in per cent of the dose at a distance of 1 cm. from the center of the longitudinal direction of the carrier.

TABLE 24.

| Distance in cm. | Dose measured in center | Dose measured halfway between center and end | Dose measured at end vertical to longitudinal axis | Dose measured at end in direction of longitudinal axis |
|---|---|---|---|---|
| 1 | 100 | 61.5 | 36.4 | 19.5 |
| 2 | 32.4 | 22.7 | 14.7 | 7.8 |
| 3 | 15.7 | 11.7 | 8.9 | 4.5 |
| 4 | 9.3 | 7.4 | 5.4 | 2.8 |
| 5 | 5.6 | 4.9 | 3.9 | 2.2 |
| 6 | 4.2 | 3.1 | 3.0 | 1.6 |
| 8 | 2.4 | 1.8 | 2.0 | 1.0 |
| 10 | 1.5 | 1.3 | 1.3 | 0.4 |

A perusal of the table confirms our assumption of the greater influence of the length of the source of radiation on the distribution of the dose. Fig. 77 presents the graph of these values.

By means of these results we are now placed in a position to plot the isodoses, i.e., the equal intensity curves for both radiation carriers. We proceeded in the manner that we took from the graphs the corre-

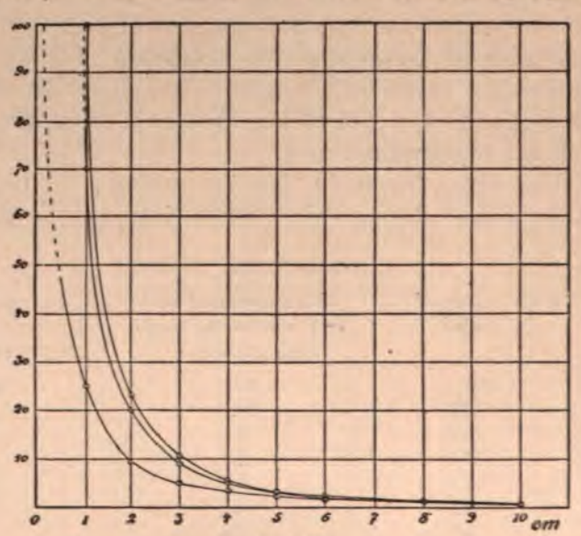



FIG. 77.

sponding distances within which the values of the dose, relative to the dose of 100 measured at a distance of 1 cm. in the center of the radiation capsules, were 90, 80, 70, 60, 50, 40, 30, 20, 10 and 5 per

cent. The values for the higher numbers have been determined by extrapolation from the course of the graphs. These values, especially for the long preparation, are fraught with a certain inaccuracy of the extrapolation and therefore cannot be plotted with any degree of exactness. In the accompanying illustrations of the isodoses the

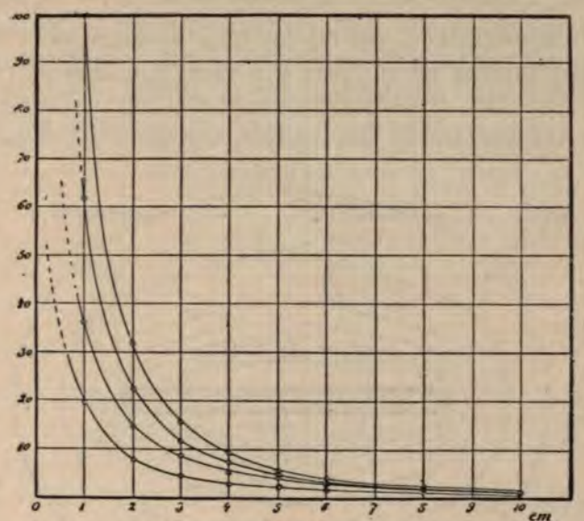



FIG. 78.

values taken from the extrapolation of the curves are entered in interrupted lines.

In Fig. 79 the isodoses of the smaller preparation are drawn in natural size. Studying the course of the curves we see that the isodoses do not run parallel to the surface of the radiation capsule. This

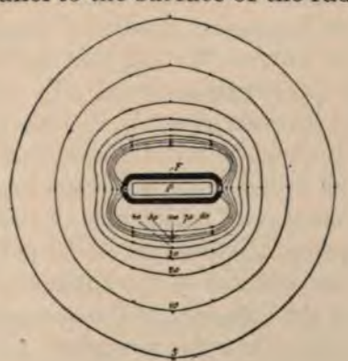


FIG. 79.

is especially seen in the curves of the higher values. The farther we move away from the radiation source the more the curves approach a circular form. The course of the isodoses at the ends is especially remarkable. The isodoses 100 and 90 enter the radiation capsule, while those of 80, 70, and so forth, approach the ends. This observation is of importance in therapy as one may deduce therefrom

that a region of tissue which lies close to the ends receives a much smaller dose than the region lying close to the center of the preparation. At the latter point according to the course of the isodose the decrease of the dose with distance is much more gradual, hence the dose applied within the same time duration is very much more intense.

Fig. 78 shows the isodoses for the long preparation. Their course close to, and farther away from the radiation source, is analogous to that in Fig. 79. The deviations of the curves from the course parallel to the surface of the capsule are much more marked.

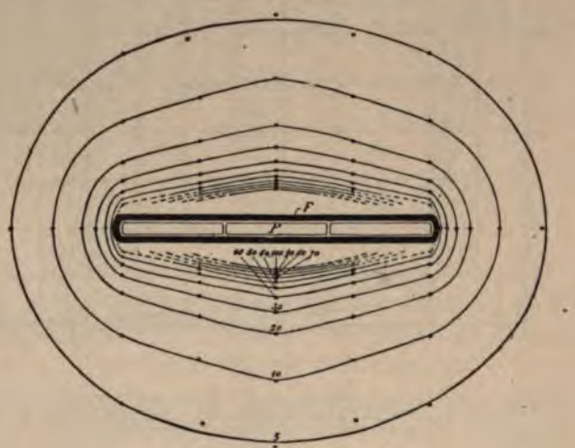


FIG. 79A.

In the observations hitherto made we have placed the dose at 100 at a distance of 1 cm. from the middle of the preparation whether measured in air or in water. We did this to be independent of the radio-activity of the preparations used. In the calculation of the dose according to the formula given in the beginning of this chapter the intensity of the impulse without absorption in 1 cm. distance is equal to the number of milligrams of radium bromid or, according to Kehrer, equal to the number of milligrams of element contained in the capsule. The absorption is calculated at 10 per cent per centimeter of tissue traversed and entered in the calculation of the dose.

The importance of the influence of the secondary rays on the dose let it appear as probable that the secondary radiation must also be considered in the absolute value of the measured dose. To prove this we conducted special tests in the manner that we determined the dose at 1 cm. distance in the phantom filled with air and then with water. In the empty phantom the time was 16.4 seconds within which the leaf of the electrometer passed through four divisions of the scale; in the filled phantom it was 15.2 seconds. The error of undesired radiations does not have to be considered in such short time periods. It is seen from these time values that the secondary radia-

tion of the radiated water does not only equalize the absorption but is about 8 per cent higher than the value calculated from the radioactive strength of the preparation. $\frac{16.4}{15.2} \times 100 = 108.$

Therefore, if we place the dose in air at 100 at 1 cm. distance from the middle of the preparation, then we must place the dose measured in water at 1 cm. distance as 108 in comparing calculated and measured doses. Table 19, therefore, must be changed as shown in the following table.

TABLE 25.

| Distance in cm. | Measured dose | Calculated dose | Difference in % of calculated dose |
|---|---|---|---|
| 1 | 108.0 | 90.0 | 20.0 |
| 2 | 25.0 | 20.26 | 23.4 |
| 3 | 11.2 | 8.1 | 38.2 |
| 4 | 5.8 | 4.1 | 41.5 |
| 5 | 3.6 | 2.36 | 52.5 |
| 6 | 2.4 | 1.48 | 62.1 |
| 8 | 1.3 | 0.65 | 100.0 |
| 10 | 0.8 | 0.35 | 130.0 |

It is self-evident that the values of the secondary radiations at a distance of 1 cm. are of a marked importance which must be expressed as a difference of the calculated and measured doses. It should not be neglected in therapeutic applications. The isodoses thereby are not changed. The following table contains the corresponding values for the long radium carrier used in these investigations.

TABLE 26.

| Distance in cm. | Measured dose | Calculated dose | Difference in % of calculated dose |
|---|---|---|---|
| 1 | 108.0 | 90.0 | 20.0 |
| 2 | 34.6 | 20.26 | 70.8 |
| 3 | 16.8 | 8.1 | 107.2 |
| 4 | 10.0 | 4.1 | 143.9 |
| 5 | 6.0 | 2.36 | 156.5 |
| 6 | 4.5 | 1.48 | 206.5 |
| 8 | 2.6 | 0.65 | 300.0 |
| 10 | 1.6 | 0.35 | 357.0 |

It follows from these investigations that the secondary rays and the geometrical size and form of the radiation capsule are of great importance in the determination of the absolute values and of the distribution of the dose in intracorporeal treatment with radium or mesothorium. These factors must always be taken in account in the propounding of biologic laws and in the conclusions based thereon.

*Conclusions:*

1. The calculation of the distribution of the dose in the intracorporeal treatment with radium from the laws of distance and absorp-

tion is incorrect, as the secondary rays arising in the radiated tissues and the geometrical form of the radium or mesothorium capsule are not considered.

2. The expression of the actual value of the dose in milligram hours of radium element is erroneous as, here also, the influence of the secondary rays is not taken into account. The value of the secondary radiation is so great that it not only equals the loss by absorption, but results in higher values for the total dose.

3. The curves of equal intensity, which have been designated "isodoses," do not take a course parallel to the circumference of the radiation capsule, but evince a course deviating quite markedly from that of the surface of the radium capsule.

# THE DETERMINATION OF EQUAL INTENSITY CURVES (ISODOSES) OF SHORT RADIUM CAPSULES

BY HENRY SCHMITZ AND ERICH HUTH*

The researches carried on by W. Friedrich and O. Glasser on the "Distribution of the Radiation Dose in Intracorporeal Radium and Mesothorium Therapy," with preparations of mesothorium capsules of a length of 2.8 cm., and a thickness of 0.46 cm. led to the observation that the geometrical size and form of the radium or mesothorium capsule and the scattered rays of the irradiated tissue are of con-

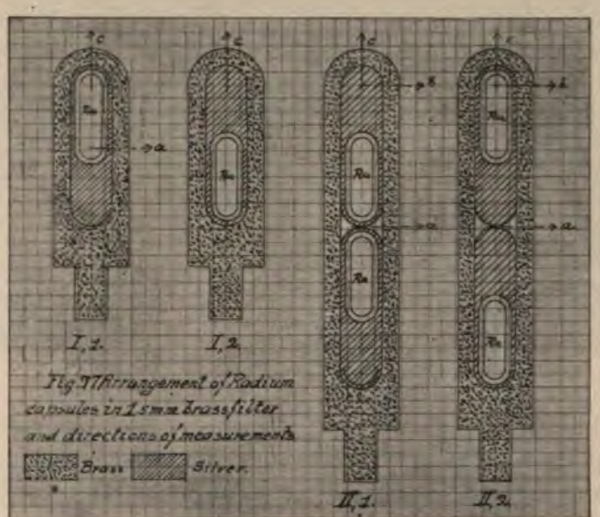



FIG. 80. (Same as Fig. 77 in German text.)

siderable importance in the distribution of the dose. It was therefore thought to be of interest to determine the course of the isodoses, i.e., the curves of equal intensities of the short radium capsules customarily used in the United States of North America.

The measurements were carried out on two capsules each possessing a radio-activity of about 25 mg. radium element. They have the following construction and dimensions: The outer silver capsule is 16 mm. long and 4 mm. in diameter. It encloses a glass tube of a length of 8 mm. and an external diameter of 2.4 mm., which contains the radium salt of a purity of + 95%. The radium fills the glass capsule firmly and uniformly. The thickness of the wall of the silver

* From the Radiologic Institute of the University Freiburg i. Br., Director Prof. W. Friedrich.

capsule is 0.5 mm. except at one end where the capsule is closed with a solid silver screwcap of a length of 7 mm. It was to be expected and confirmed by the investigations that the heavy silver screwcap would have a marked influence on the course of isodoses or equal intensity curves. The radium capsules were enclosed in a brass filter

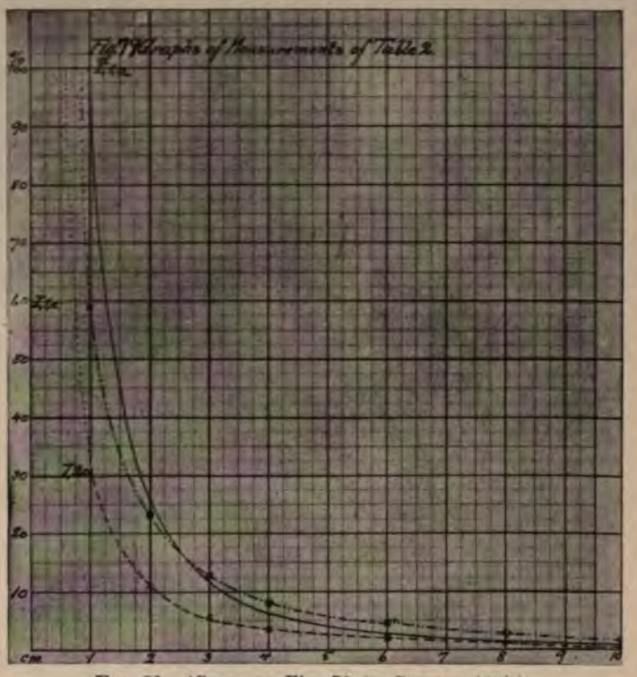


FIG. 81. (Same as Fig. 79 in German text.)

of a wall thickness of 1.5 mm. as is customarily done in therapeutic radium applications. Fig. 80 represents the arrangement of the capsules in the filters and also indicates the directions in which the intensities and their decrease with increasing distance were measured. If only one capsule was used then the distribution of the dose was measured in the direction of the longitudinal axis at both ends, that is, the end formed of 0.5 mm. silver and the one closed with the 7 mm. silver screwcap. If both preparations were used then the two silver capsules were arranged in the brass filter so that at one time the two silver screwcaps were placed at the ends and at another time in the center as seen in Fig. 80.

The details of the measurements were essentially the same as those employed and described by Friedrich and Glasser in the preceding chapter. The radium preparations were placed in a water phantom during the measurements. They were surrounded on all sides with a layer of water at least 10 cm. thick. Thereby the same conditions of absorption were maintained as in intracorporeal radium therapy since the absorption of the gamma- and scattered-rays in water is in the mean the same as that in human tissue. A small ioniza-

tion chamber of a volume of 0.5 ccm. was placed in the middle of the glass jar. The radium capsule could be brought in every desired position in relation to the ionization chamber by moving it along

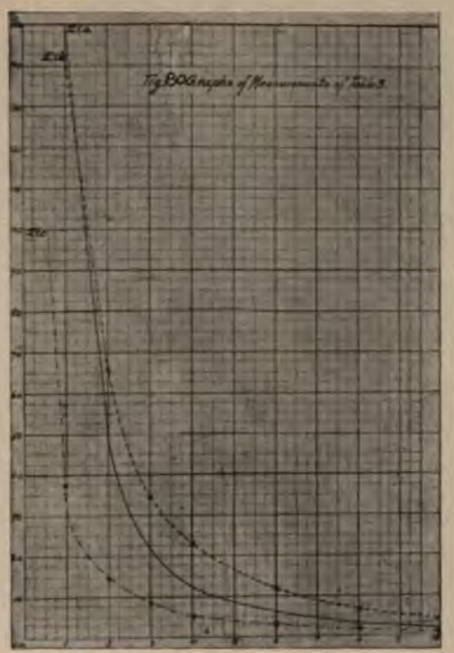


FIG. 82. (Same as Fig. 80 in German text.)

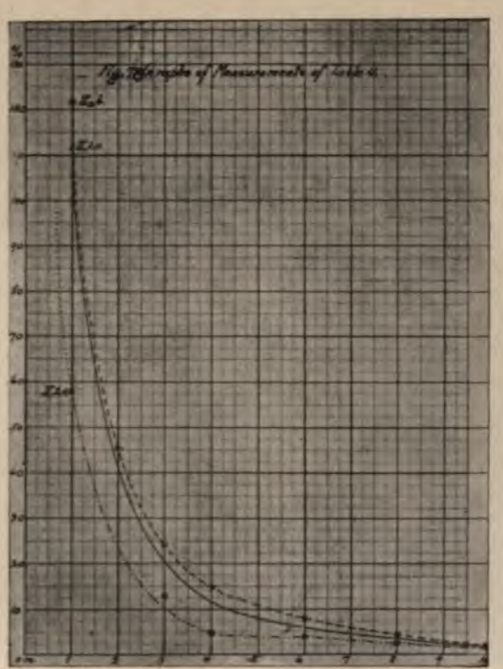


FIG. 83. (Same as Fig. 78 in German text.)

horizontal and vertical slides. The distances of the capsule from the chamber could be determined by millimeter measures attached to the slides. One of the electrodes of the ionization chamber was

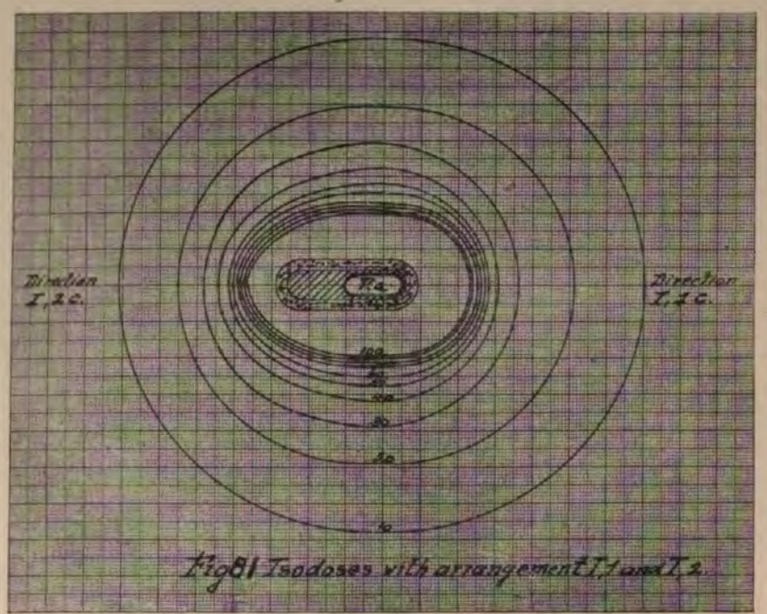



FIG. 84. (Same as Fig. 81 in German text.)

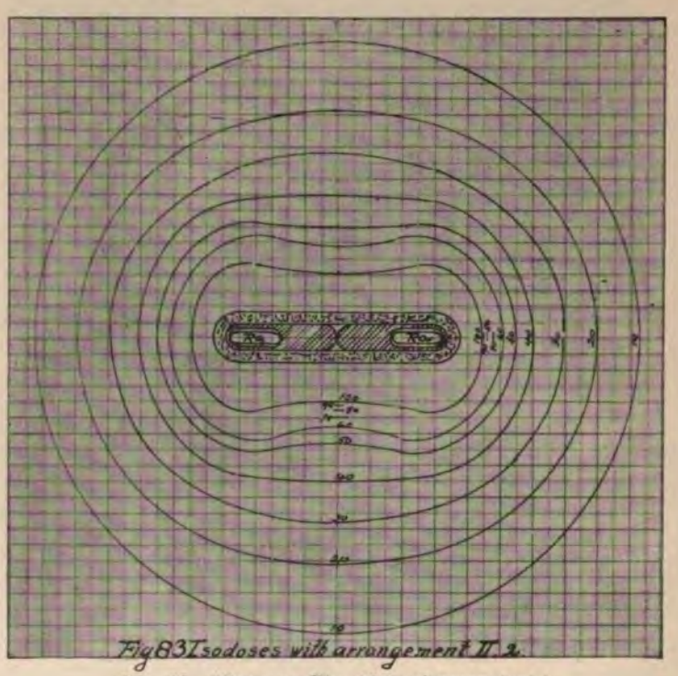



FIG. 85. (Same as Fig. 83 in German text.)

connected with a storage battery of 160 volts, the other was connected to the electrometer with a brass wire conducted through a brass tube 1.5 meters long and insulated with powdered c. p. sulphur, which was carefully and firmly packed in the brass tube to exclude all the air from the insulation. The electrometer was kept at a voltage of 360 by a storage battery. It was placed in a box of thick pasteboard covered with zinc sheeting, which was grounded. This box was surrounded by a larger one covered with tinfoil. The space between the two boxes was firmly packed with cotton to protect the electrometer

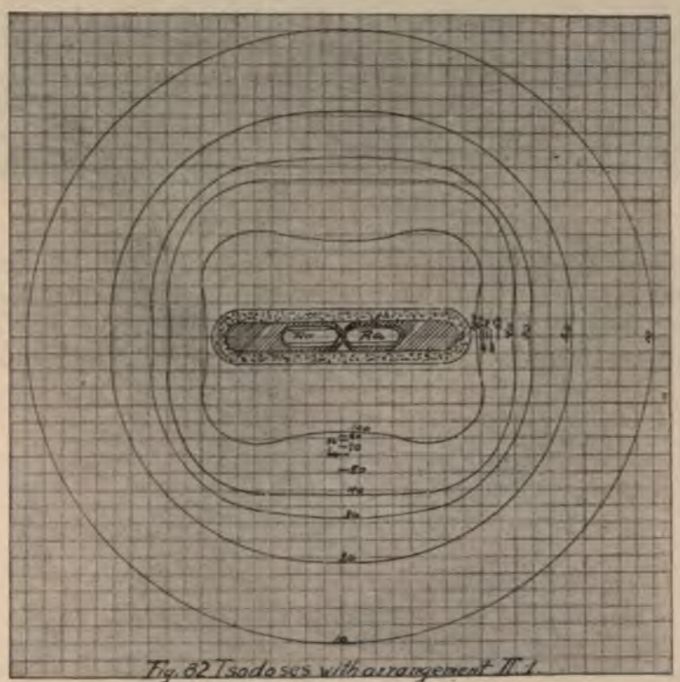



FIG. 86. (Same as Fig. 82 in German text.)

as much as possible from external influences of temperature and moisture. See Figs. 75 and 76.

The time was observed within which the gold leaf of the electrometer by a charge through the ionization current passed through five divisions of the scale contained in a reading microscope. The observed time periods are inversely proportional to the dose which an area in the body corresponding in size to the volume of the ionization chamber receives within the same time. The sources of errors always present in such an apparatus have been fully considered in the monograph of Friedrich and Glasser. The undesired radiation must always be taken into consideration. It results from the action of the rays on the conductors and the electrometer whereby the discharge of the gold leaf is accelerated. The undesired radiation was determined before and after each series of measurements and entered in the final calculation of the measurements.

taking into account any change in sensitiveness of the apparatus. Finally the values for the decrease of the dose with distance previously obained were correspondingly corrected and expressed in percentages of the dose in the direction I, 1, a, Fig. 80. The following table is an example of a complete series of measurements with the final computation of the comparative values. Tables 28, 29 and 30 give the corrected and the final comparative values for all the directions indicated in Fig. 80.

The distances were next entered on the abscissa and the percentages on the ordinate and the final values of intensities entered,

Table 4. Results of Measurements in Directions

| Distance in Cm. | I, 2, a. A. | I, 2, a. B. | I, 2, b. A. | I, 2, b. B. | I, 2, c. A. | I, 2, c. B. |
|---|---|---|---|---|---|---|
| 1 | 100 | 110,8 | 100 | 122,0 | 100 | 57,6 |
| 2 | 38,1 | 42,2 | 37,4 | 45,6 | 40,6 | 23,2 |
| 3 | 19,0 | 21,0 | 19,8 | 24,2 | 22,2 | 10,9 |
| 4 | 11,1 | 12,3 | 12,1 | 14,7 | 12,5 | 4,5 |
| 6 | 5,5 | 6,1 | 6,1 | 7,4 | 6,7 | 3,2 |
| 8 | 3,0 | 3,3 | 3,4 | 4,2 | 4,2 | 2,2 |
| 10 | 2,0 | 2,2 | 2,2 | 2,7 | 2,7 | 1,6 |

TABLE 30. (Same as Table 4 in German text.)

given under B in Tables 28, 29, 30. See Figs. 83, 81 and 80. From the graphs thus constructed the distances in centimeters were taken at which the doses or intensities amounted to 100, 90, 80, 70, 60, 50, 40, 30, 20 and 10 per cent. The values in centimeters were then plotted to construct the curves of equal intensities or isodoses as seen in Figs. 84, 85 and 86. Values greater than measured must be plotted by extrapolation, hence can only be given with an approximate exactness.

Studying the results obtained it is seen that in one of the preparations, namely I, 1 a, the decrease of the dose with increase in distance measured in the center vertically to the longitudinal axis corresponds almost exactly to the decrease of intensity calculated from the law of squares. In this particular instance the increase in the dose due to the scattered rays in the irradiated water is apparently equal to the decrease of the intensity caused by absorption in water. When using one radium capsule the isodoses run an oval course within a short distance from the radiation source and then approach rapidly the form of a sphere at the low percentages of 30, 20 and 10. The oval course of the isodoses and the eccentric position

of the radium capsule therein must be attributed to the secondary rays emitted from the massive silver screwcap which must be considerable in proportion to the total radiation. This is substantiated by the observation that the isodoses 30, 20 and 10 mm. run practically concentric in reference to the center of the radium salts R. The isodoses for the higher percentages in the direction of the longitudinal axis do not enter the capsule proper as they do in those obtained by Friedrich and Glasser. This may be explained by the considerably higher ratio existing between the length and the diameter of the radium capsules. The ratio is 3.33 to 1 in comparison to that of the German preparations which is about 6 to 1.

The course of the isodoses is especially noteworthy when two radium capsules in a filter are used. It almost approaches a rectangle for the values 100 to 40 and probably results from the action of the secondary rays arising in the solid silver cap. That the softer secondary radiation of the silver is concerned appears to be substantiated by the more rapid decrease in the intensity of the radiation at the corresponding portion of the curves.

It is also evident that the special form and construction of the radium capsules, especially when a combination of two capsules is used are responsible for a remarkably uniform distribution of the dose in tissues. For instance, if two radium capsules are arranged as in Fig. 86, then an almost equal distribution of intensity is attained on the surface of a cylinder of a length of 4.5 cm. and a diameter of 2 cm. corresponding to the isodose 100. With the arrangement of Fig. 85 the same isodose forms a cylinder of a length of 4 cm. and a width of 3 cm.

# THE IMPORTANCE OF FILTRATION ON THE DOSE IN INTRACORPOREAL APPLICATIONS OF RADIUM AND MESOTHORIUM*

BY OTTO GLASSER

The use of filters in radium and mesothorium therapy is necessary to arrest the soft components of the radiation and thereby avoid the undesirably intense surface action and improve the quotient of the dose. A variety of metals has been selected for this purpose; the selection was based on purely empirical observations. Such an empirical method is fraught with a number of uncontrollable factors which may play an important rôle and contribute to undesirable and dangerous side actions in therapy. One of these factors is the secondary radiation arising in the filter. Its influence on the deep dose has as yet not been clearly explained. To interpret its significance one must possess a knowledge of the different components of the secondary filter radiation and of their participation in the deep dose.

The filters are employed to arrest the primary soft beta rays which possess a low penetration and thereby prevent their absorption in the upper layers of the surface tissue. Metal filters have been chosen for this purpose, mainly for practical reasons as thereby the thickness of the filters may be markedly reduced. Besides the primary gamma-rays, the different components of the secondary radiations emerge from the filters. These are:

1, the scattered rays,

2, the secondary beta or corpuscular rays, and

3, the characteristic secondary rays.

A study of these components in relation to the atomic weights of the filters will furnish an idea of their influence on the deep dose.

Scattered rays form when the projected primary rays strike the atoms of the filter. The primary rays are thereby deflected from their straight paths emerging in all directions. The hardness of the scattered rays is the same as that of the projected primary rays. The influence of the scattered rays on the size of the deep dose depends on the atomic weights of the filter substance. The higher the atomic weight, the larger is the scattering coefficient and the greater also is the absorption of the scattered rays in the filter substance. Consequently the total sum of scattered rays emerging from filters of low atomic weight is greater than that of filters of high atomic

* Strahlentherapie, Vol. XII, 1921, page 256.

weight. This fact plays a very important rôle in deep therapy and we call attention to the exceedingly important increase in the size of the dose due to the influence of the scattered radiation in human tissue as shown in the reports on radium and X-rays of Kroenig and Friedrich,[1] Seitz and Wintz, Glocker, and O. Glasser.[2]

The secondary beta-rays also arise in the filter. They are very soft. All of the secondary beta-rays, except those forming in the most peripheral parts of the filter are absorbed in the latter. The beta-rays of the outer layers of the filter emerge and become active in the immediate neighborhood. If the filter is in actual contact with human tissue, then the soft secondary beta-rays are absorbed in the most superficial layers of the human tissue, where they exert an intense biologic action, as has been experimentally proven by Kroenig and Friedrich. In deep therapy it is therefore necessary to reduce to a minimum the beta-rays by an additional filter of celluloid or pure rubber. The secondary beta-rays do not possess any influence on the size of the deep dose on account of their great absorbability. The hardness of the secondary beta-rays is also dependent on the atomic weight of the filter—it increases with an increase in the atomic weight.

The characteristic secondary radiation is set up in the filter. Every element that is struck by a radiation of a hardness characteristic for the same is capable of emitting a characteristic radiation if the exciting primary radiation is of a shorter wave length than the excited secondary characteristic radiation. The hardness of the latter generally increases with an increase in the atomic weight of the filter. Numerous investigations[3] and theoretical discussions[4] have dealt with the influence of the characteristic radiations on the deep dose. It appears that the importance of the characteristic radiation has been very much exaggerated. However, the basis for the theoretical discussion of Grossmann, and the biologic investigations of Kroenig and Friedrich, and of R. Lenk, form exceptions. They arrived by means of biologic experiments at similar results as were obtained by the physical investigations described in this paper. From a purely physical standpoint it appears that the characteristic radiations cannot appreciably increase the deep dose.

Another matter of importance is the influence of the increase of the geometrical size and shape of the radio-active source—which have become considerably augmented by the characteristic filter rays—on the decrease of the dose with distance in the depth. Friedrich and Glasser in the paper mentioned referred to the fact that the decrease

[1] B. Kroenig and W. Friedrich: "Die physikalischen und biologischen Grundlagen der Strahlentherapie." English Translation, Rebman Company, New York.

[2] W. Friedrich und O. Glasser: "Über die Dosenverhältnisse bei intrakorporaler Radium und Mesothoriumtherapie." Strahlentherapie, 1920, Vol. 10, page 20.

[3] R. Lenk, Zur Frage der Filtersekundärstrahlen. Strahlentherapie. Kroeniggedenk, band 11 (Vol. 2, page 1), 1920.

[4] W. Friedrich und O. Glasser, Strahlentherapie, 1920. (Vol. 2, page 20.)

of the dose of radio-active substances depends on the geometrical form of the radio-active capsule as well as on distance, absorption and scattered radiation. Since the characteristic radiation of the filter causes an increase in the size of the radiation source, it will be instrumental in bringing about a decrease of the intensity of the dose in the deeper tissue different from that of a capsule which has been inserted in a filter devoid of characteristic rays.

Considering the purpose and action of the filtration of radio-active substances and the influence on the deep dose, it may be stated that the soft beta- and some hard gamma-rays components are arrested by filtering. In deep therapy the thickness and atomic weight of the filter are selected so that only the hard gamma-rays pass through the filter, while the softer rays are arrested. The hard gamma-rays and the scattered radiation essentially determine the size of the deep dose. The characteristic radiation of the filter material may also participate in the production of the deep dose. The primary and secondary beta-rays are reduced to a negligible quantity (by means of a filter and an accessory celluloid filter), thereby avoiding injury to the surface tissue. They have not any influence on the size of the deep dose.

Investigations were performed to determine experimentally the correctness of these conclusions. Filters of extreme thicknesses and of high atomic weights were used (lead filters of 0.8 and 10 mm., brass filters of 1.5 mm. and aluminum filters of 10 mm. thickness).

The same method of investigation was used for these experiments as had been employed in the determination of the distribution of the radiation dose in tissue described in detail on a previous page. The procedure is based on the ionization method.

The measurements were performed as follows: A preparation of mesothorium equivalent to 45.5 mg. radium element, enclosed in a silver capsule of a length of 22.5 mm., was inserted in a brass filter capsule of a wall thickness of 1.5 mm. The center of the long side was placed at a distance of 2 cm. from the center of the ionization chamber. The time was then measured within which the leaf of the electrometer passed through five divisions of the scale. Next, the brass filter capsule was exchanged for an aluminum filter capsule of a wall thickness of 10 mm., then a lead filter of 10 mm., and finally one of 0.8 mm. The filters were placed exactly as in the first measurement and the time measured for equal excursions of the leaf of the electrometer.

The influence of the sources of errors (undesired radiation, dielectric and insulation defects) on the excursion of the leaf of the electrometer was determined and considered in the calculation of the results. The resultant values are: If the charging time for five divisions of the scale, by the mesothorium capsule inserted in a 1.5 mm. brass filter equals 1, then the time for a 10 mm. aluminum filter is 0.9, for 0.8 mm. lead 1.08, and for 10 mm. lead 1.75. These values

conform closely to those obtained by W. Friedrich with the biologic method.

The radiation filtered through heavy lead of high atomic weight suffers a considerable loss. An influence of the characteristic lead rays on the dose is not discernible at a distance of 2 cm.

It is not possible to state from these results whether a characteristic lead radiation is excited or whether its influence on the dose cannot be recognized due to certain factors, for instance absorption. To answer these questions a determination of the decrease of the dose with distance was made. The capsule, inserted in a filter, was carefully placed at known distances from the ionization chamber and the time necessary for the excursion of the leaf through five divisions of the scale determined for each distance. The details of the measurements and the amount of the sources of errors, and so forth, were the same as in the previous measurements. The same capsule of mesothorium was used. A difficulty arose from the fact that the center of the capsule could not be placed at the distance of 1 cm. from the ionization chamber on account of the thickness of the filters. For this reason the measurements were begun at a distance of 2 cm. The values obtained at 3, 4, 5, 6, 8 and 10 cm. respectively were expressed in percentages of the values at 2 cm. The first column gives the distances in centimeters between the center of the capsule and the ionization chamber; the second column represents the values of the dose at the various distances for the capsule filtered with 10 mm. lead in per cent of the dose at a distance of 2 cm. In column three the corresponding values of the dose for the preparation filtered with 1.5 mm. brass are contained.

TABLE 31.

| 1. Distance in cm. | 2. Dose for capsule filtered with 10 mm. lead | 3. Dose for capsule filtered with 1.5 mm. brass |
|---|---|---|
| 2 | 100.0 | 100.0 |
| 3 | 40.2 | 44.8 |
| 4 | 20.0 | 23.3 |
| 5 | 12.6 | 14.2 |
| 6 | 8.9 | 9.5 |
| 8 | 4.8 | 5.5 |
| 10 | 2.3 | 3.3 |

From the table may be seen that if the dose obtained at 2 cm. with the lead as well as brass filter is placed at 100 and the doses at the other distances are expressed in per cent of the 2 cm. values, then the values of the doses for the rays filtered with lead decrease more rapidly with distance than those for rays filtered with brass. If a characteristic radiation is excited in the lead then the more rapid decrease of the lead filtered rays as determined by these experiments may be explained as follows: The rays after passing through the lead contain a larger percentage of soft rays than the brass filtered rays. The stronger absorption in the tissues of the soft rays results in a more rapid decrease of intensity.

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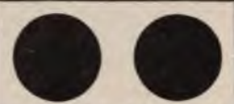
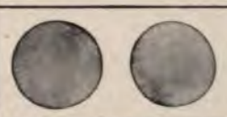
| Kind of Ray | $h_1$ in mm Al. | D = 15 e | D = 30 e |
|---|---|---|---|
| Unfiltered X-rays | 2.2 | | |
| X-rays filtered with 3 mm Al. | 4.3 | | |
| X-rays filtered with 10 mm Al. | 6.9 | |  |
| X-rays filtered with 1 mm Copper. | 10.5 | | |
| Gamma-rays | 50 |  | |

FIG. 1.

Comparison of Kienböck dosimeter with the improved Iontoquantimeter.

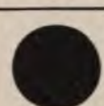
| D = 15 e | D = 22.5 e | D = 30 e |
|---|---|---|
| | | |
|  | | |

FIG. 2.

Sensitiveness of Kienböck dosimeter.

REBMAN COMPANY, NEW YORK

*Day of Radiation: June 25.*

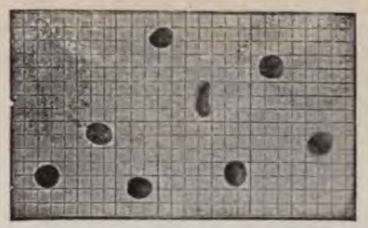


FIG. 1. Starting material.

Observation 3 days after the beginning of radiation.

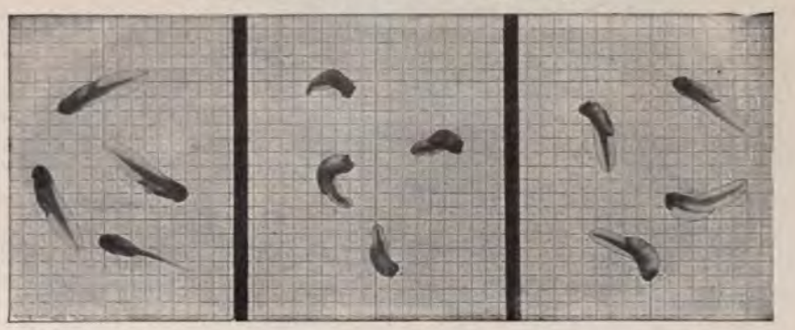


FIG. 2. Controls. Radiation dose=200 e. Radiation dose=100 e.

Observation 5 days after the beginning of radiation.

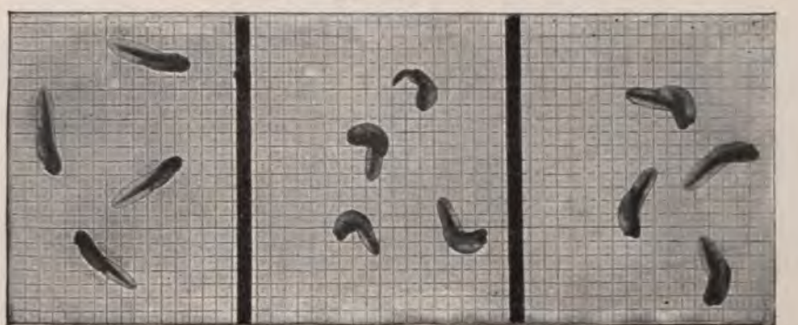


FIG. 3. Controls. Radiation dose=200 e. Radiation dose=100 e.

Observation 8 days after the beginning of radiation.

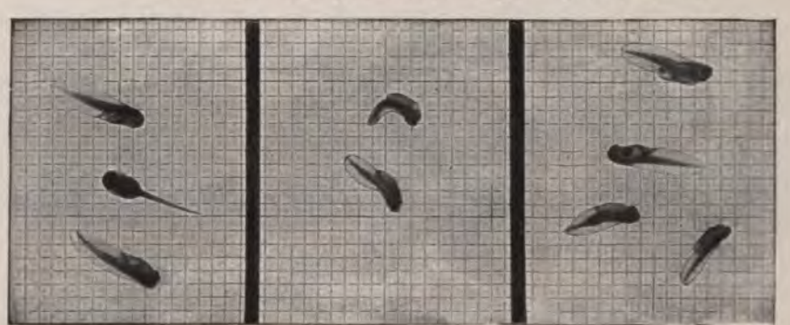


FIG. 4. Controls. Radiation dose=200 e. Radiation dose=100 e.

Experiments on sensitiveness of frog larvæ to the action of heavy filtered X-rays.

REBMAN COMPANY, NEW YORK

*Day of Radiation:*
*June 8.*

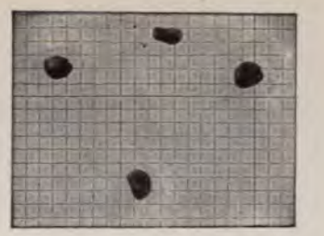


FIG. 1. Starting material.

Observations 6 days after radiation.

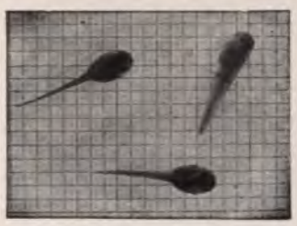


FIG. 2. Controls.

FIG. 3. X-rays filtered with 3 mm Al.

FIG. 4. X-rays filtered with 1 mm Copper.

Observation 14 days after radiation.

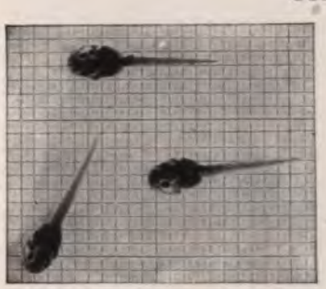


FIG. 5. Controls.

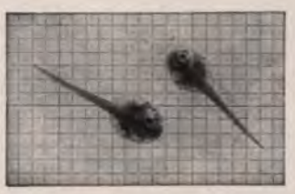


FIG. 6. X-rays filtered with 3 mm Al.

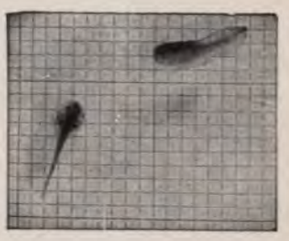


FIG. 7. X-rays filtered with 1 mm Copper.

Observation 16 days after radiation.

FIG. 8. Controls.

FIG. 9. X-rays filtered with 3 mm Al.

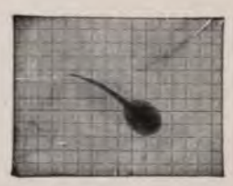


FIG. 10. X-rays filtered with 1 mm Copper.

Comparison of experiments on the intensity of the biological action of X-rays filtered with 3 mm Aluminum and 1 mm Copper. Dose determined with Aluminum chamber dosimeter.

REBMAN COMPANY, NEW YORK

*Kroenig-Friedrich*

***Day of Radiation:***
***May 31.***

(Dosation with Aluminum chamber dosimeter.)

REBMAN COMPANY, NEW YORK

## *Days of Radiation: April 19 and 20.*

Findings 14 days after radiation.

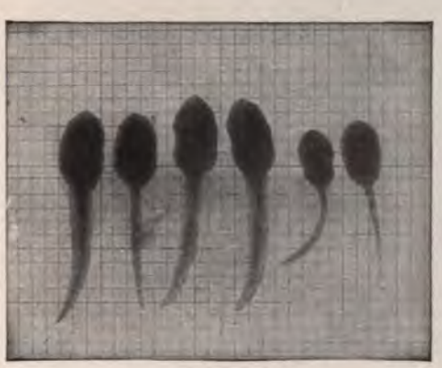


FIG. 1.

Left: Two larvæ rayed with X-rays filtered with 1 mm Copper.
Middle: Two controls.
Right: Two larvæ exposed to gamma-rays.

Findings 24 days after radiation.

FIG. 2.

Left: Two larvæ exposed to gamma-rays.
Middle: Two controls.
Right: Two larvæ rayed with X-rays filtered through 1 mm Copper.

Findings 28 days after radiation.

FIG. 3.

Left: Two larvæ rayed with X-rays filtered with 1 mm Copper.
Middle: Two controls.
Right: Two larvæ exposed to gamma-rays.

Findings 60 days after radiation.

FIG. 4.

Left: 1 larva rayed with X-rays filtered with 1 mm Copper.
Right: 1 control.

Comparison of investigations on the intensity of the biologic action of gamma-rays of mesothorium resp. radium filtered with 1.5 mm brass + 5 mm celluloid and X-rays filtered with 1 mm Copper.

(Dosation with Aluminum chamber dosimeter.)

REBMAN COMPANY, NEW YORK

*Day of Radiation: June 25.*

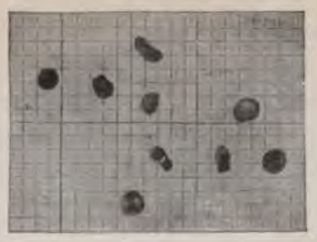


Fig. 1. Starting material.

Observation 3 days after radiation.

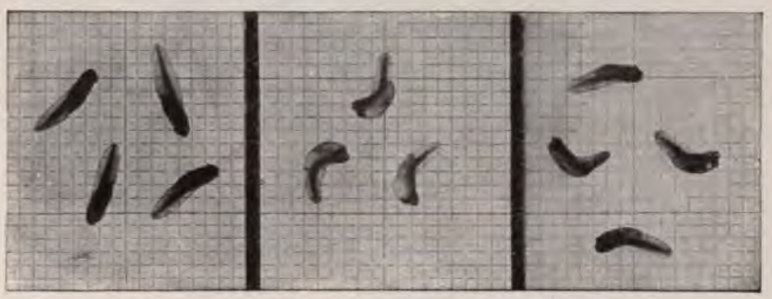


Fig. 2. Controls. Fig. 3. X-rays filtered with 3 mm Al. Fig. 4. X-rays filtered with 1 mm Copper.

Observation 7 days after radiation.

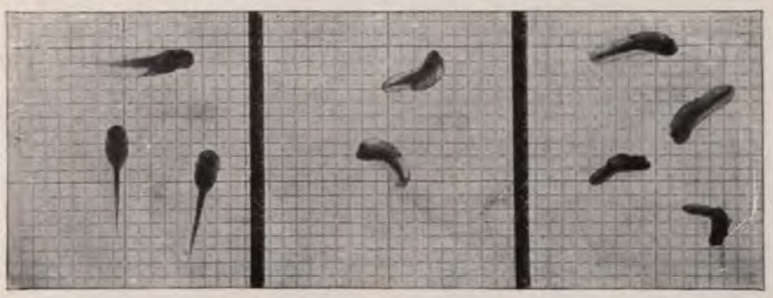


Fig. 5. Controls. Fig. 6. X-rays filtered with 3 mm Al. Fig. 7. X-rays filtered with 1 mm Copper.

Observation 10 days after radiation.

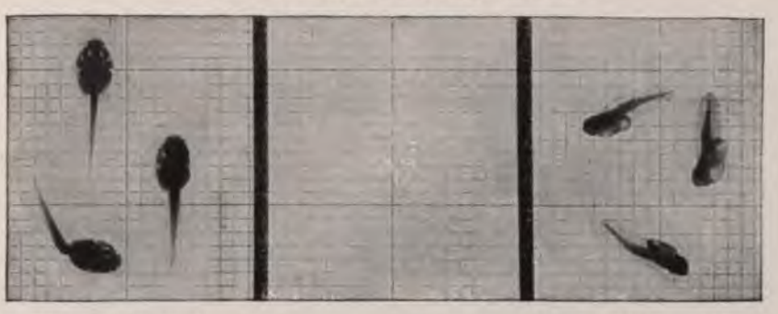


Fig. 8. Controls. Fig. 9. X-rays filtered with 1 mm Copper.

Determination of the biologic factor of X-rays filtered with 3 mm Al. and 1 mm Copper.

(Dosation with Aluminum chamber dosimeter.)

REBMAN COMPANY, NEW YORK

*Day of Radiation: March 7.*

FIG. 1. Starting material.

Findings 2 days after radiation.

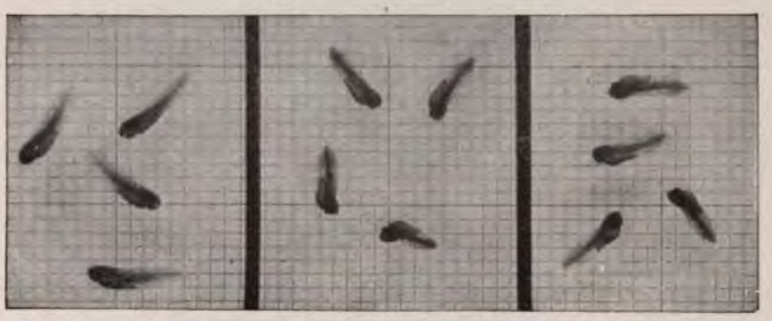


FIG. 2. Controls. Gamma-rays. Dose=80 e. X-rays filtered with 1 mm Copper. Dose=320 e.

Findings 5 days after radiation.

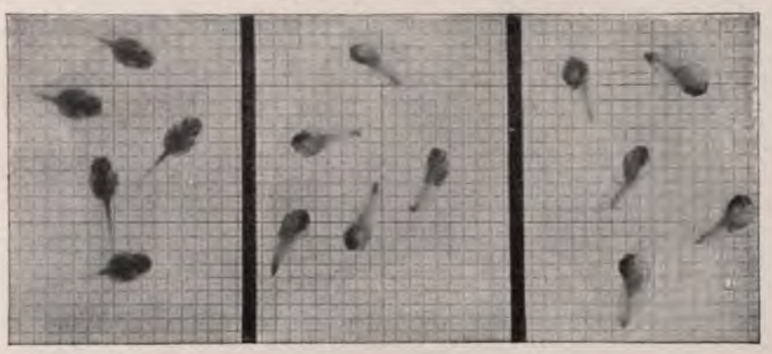


FIG. 3. Controls. Gamma-rays. Dose=80 e. X-rays filtered with 1 mm Copper. Dose=320 e.

Findings 7 days after radiation.

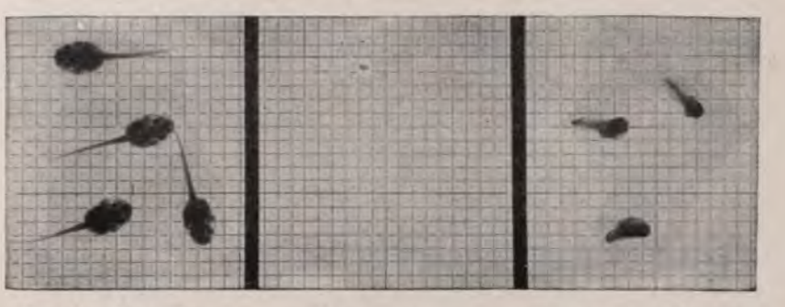


FIG. 4. Controls. Gamma-rays. Dose=80 e. X-rays filtered with 1 mm Copper. Dose=320 e.

Determination of the biologic factor of gamma-rays of radium resp. mesothorium filtered through 1.5 mm brass + 5 mm celluloid and X-rays filtered with 1 mm Copper.

(Dosation with Aluminum chamber dosimeter.)

REBMAN COMPANY, NEW YORK

*Day of radiation: Sept. 10. 1916.*

Findings 35 days after radiation.

Fig. 1. Dose = 145 e.

Findings 35 days after radiation.

Fig. 2. Dose = 185 e.

Observations on the sensibility of the human skin to the action of filtered X-rays.

*Rebman Company — New York.*

*Day of radiation: Sept. 20. 1915.*

Findings 47 days after raying.

Fig. 1. X-rays filtered with 1 mm copper.

Fig. 2. X-rays filtered with 3 mm aluminum.

Findings 47 days after raying.

Findings 58 days after raying.

Fig. 3. X-rays filtered with 1 mm copper.

Fig. 4. X-rays filtered with 3 mm aluminum.

Findings 58 days after raying.

Comparison of observations on the intensity of the biologic action of X-rays filtered with 3 mm aluminum and 1 mm copper. (Dosation with aluminum chamber dosimeter.)

*Rebman Company — New York.*

*Day of radiation: Sept. 11. 1915.*

Findings 45 days after raying.

Fig. 1. X-rays filtered with 1 mm copper.

*Day of radiation: Sept. 16. 1915.*

Findings 40 days after raying.

Fig. 2. X-rays filtered with 3 mm aluminum.

Findings 67 days after raying.

Fig. 3. X-rays filtered with 1 mm copper.

Findings 62 days after raying.

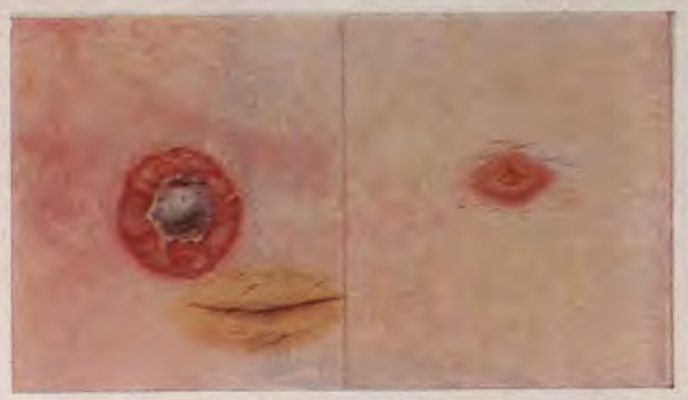
Fig. 4. X-rays filtered with 3 mm aluminum.

Comparison of observations on the intensity of the biologic action of X-rays filtered with 3 mm aluminum and 1 mm copper on the skin. (Dosation with aluminum chamber dosimeter.)

*Rebman Company — New York.*

*Day of radiation: July 22. 1915.*

Findings on day of raying.



Findings on day of raying.

Fig. 1. X-rays filtered with 1 mm copper.

Fig. 2. X-rays filtered with 3 mm aluminum.

Findings 55 days after raying.

Findings 55 days after raying.

Fig. 3. X-rays filtered with 1 mm copper.

Fig. 4. X-rays filtered with 3 mm aluminum.

Comparative observations on the intensity of the biologic action of X-rays filtered with 3 mm aluminum and 1 mm copper on skincancers. (Dosation with aluminum chamber dosimeter.)

*Rebman Company — New York.*

Case 1. Mrs. G.

Findings on day of radiation.

Case 2. Mrs. F.

Findings on day of radiation.

(Dosation with graphite chamber dosimeter.)

REBMAN COMPANY, NEW YORK

Case 1. Mrs. G.

Case 2. Mrs. F.

Findings on day of radiation.

Fig. 1. Radiation with X-rays filtered with 1 mm copper.

Fig. 4. Radiation with gamma rays of radium resp. mesothorium filtered with 1·5 mm brass + 5 mm celluloid.

Findings on day of radiation.

Findings 74 days after radiation.

Fig. 2. Radiation with X-rays filtered with 1 mm copper.

Fig. 5. Radiation with gamma rays of radium resp. mesothorium filtered with 1·5 mm brass + 5 mm celluloid.

Findings 34 days after radiation.

Findings 148 days after radiation.

Findings 281 days after radiation.

*Day of Radiation: April 28.*

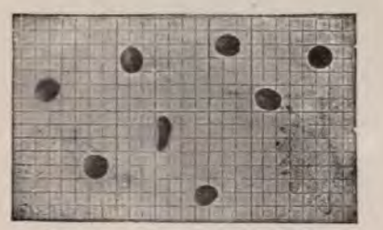


FIG. 1. Starting material.

Findings 10 days after radiation.

FIG. 2. Controls. Gamma-rays. X-rays filtered with 1 mm Copper.

Comparative observations on the intensity of the biologic action of gamma-rays of radium resp. mesothorium filtered with 1.5 mm brass + 5 mm celluloid and X-rays filtered with 1 mm Copper.

(Dosation with graphite chamber dosimeter.)

REBMAN COMPANY, NEW YORK

*Dosation with aluminum chamber.*

*Day of Radiation:*
*December 5.*

Fig. 1. Starting material.

Findings 14 days after radiation.

Fig. 2.

Findings 21 days after radiation.

Fig. 3.

From left to right the controls are seen in the first field, the beans radiated with gamma-rays in the second field, and those radiated with X-rays filtered with 1 mm Copper in the third field.

REBMAN COMPANY, NEW YORK

*Dosation with graphite chamber.*

*Day of Radiation:*
*December 14.*

Fig. 1. Starting material.

Findings 14 days after radiation.

Fig. 2.

Findings 21 days after radiation.

Fig. 3.

From left to right the controls are seen in the first field, the beans rayed with gamma-rays in the second field, and those exposed to X-rays filtered with 1 mm Copper in the third field.

REBMAN COMPANY, NEW YORK

*Days of raying: November 5. to 7. 1915.*

Findings 10 days after radiation.

Findings 10 days after radiation.

REBMAN COMPANY, NEW YORK

*Days of radiation: Jan. 29. to Feb. 1. 1916.* *Days of radiation: Jan. 29. to Feb. 5. 1916.*

Findings 8 days after radiation.

Fig. 1. Gamma rays.

Fig. 2. Beta rays.

Findings 3 days after radiation.

*Rebman Company — New York.*

REBMAN COMPANY, NEW YORK

of filtered X-rays of like dose, like lightintermissions, but different inte
and time duration of application.

*Rebman Company — New York.*

REBMAN COMPANY, NEW YORK

*Day of radiation: Nov. 6. 1916.*

Findings 28 days after radiation.

Fig. 1. Radiation with small intensity.

Fig. 2. Radiation with large intensity.

Findings 28 days after radiation.

Findings 35 days after radiation.

Fig. 3. Radiation with small intensity.

Fig. 4. Radiation with large intensity.

Findings 35 days after radiation.

Findings 57 days after radiation.

Fig. 5. Radiation with small intensity.

Fig. 6. Radiation with large intensity.

Findings 57 days after radiation.

Comparative observations on the intensity of the biologic action on the skin of filtered X-rays of like dose, like lightintermissions, but different intensity and time duration of application.

*Rebman Company — New York.*

REBMAN COMPANY, NEW YORK

## *Day of Radiation: May 24.*

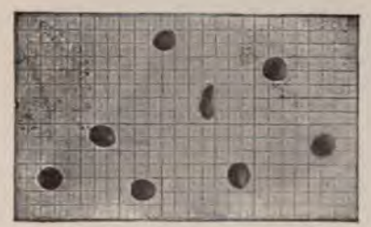


FIG. 1. Starting material.

Findings 9 days after radiation.

FIG. 2. Controls. Radiation with unipulse-instrumentarium. Radiation with apex-instrumentarium.

Findings 17 days after radiation.

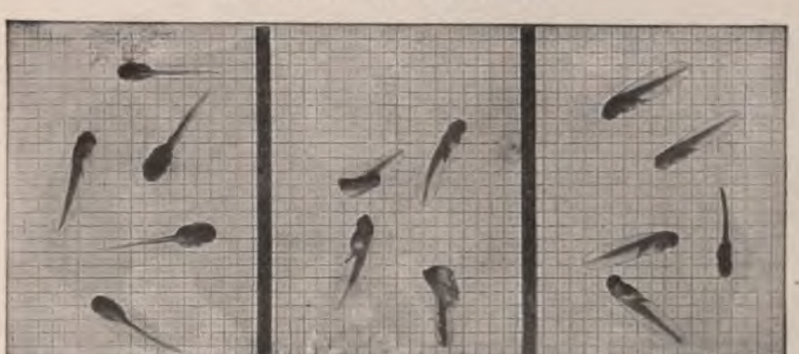


FIG. 3. Controls. Radiation with unipulse-instrumentarium. Radiation with apex-instrumentarium.

Comparative observations on the intensity of the biologic action of filtered X-rays of like doses, like duration of application but different intensities and light interruptions.

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*Day of radiation: Sept. 25. 1915.* *Days of radiation: Sept. 29. to Oct. 11. 1915.*

Findings 31 days after radiation.

Fig. 1. One sitting.

Fig. 2. Interrupted sittings.

Findings 15 days after radiation.

Findings 41 days after radiation.

Fig. 3. One sitting.

Fig. 4. Interrupted sittings.

Findings 25 days after radiation.

Findings 53 days after radiation.

Fig. 5. One sitting.

Fig. 6. Interrupted sittings.

Findings 37 days after radiation.

Comparative observations on the intensity of the biologic action of X-rays on the skin in one and interrupted dose.

*Days of radiation: Mch. 22. to 24. 1915.*

Findings 10 days after radiation.

Fig. 1. Radium rays.

Fig. 2. Mesothorium rays.

Findings 10 days after radiation.

Findings 18 days after radiation.

Findings

*Days of radiation: Sept. 13. and 14. 1916.*

Fig. 1.
Findings on the day of radiation.

Fig. 2.
Findings 68 days after radiation.

Observation on the biologic action of X-rays filtered with 1 mm copper on a carcinoma of the scalp.

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*Days of radiation: Aug. 22. 1916.*

Fig. 1.
Findings on day of radiation.

Fig. 2.
Findings 41 days after radiation.

Observation on the biologic action of X-rays filtered with 1 mm copper on a carcinoma of the vulva.

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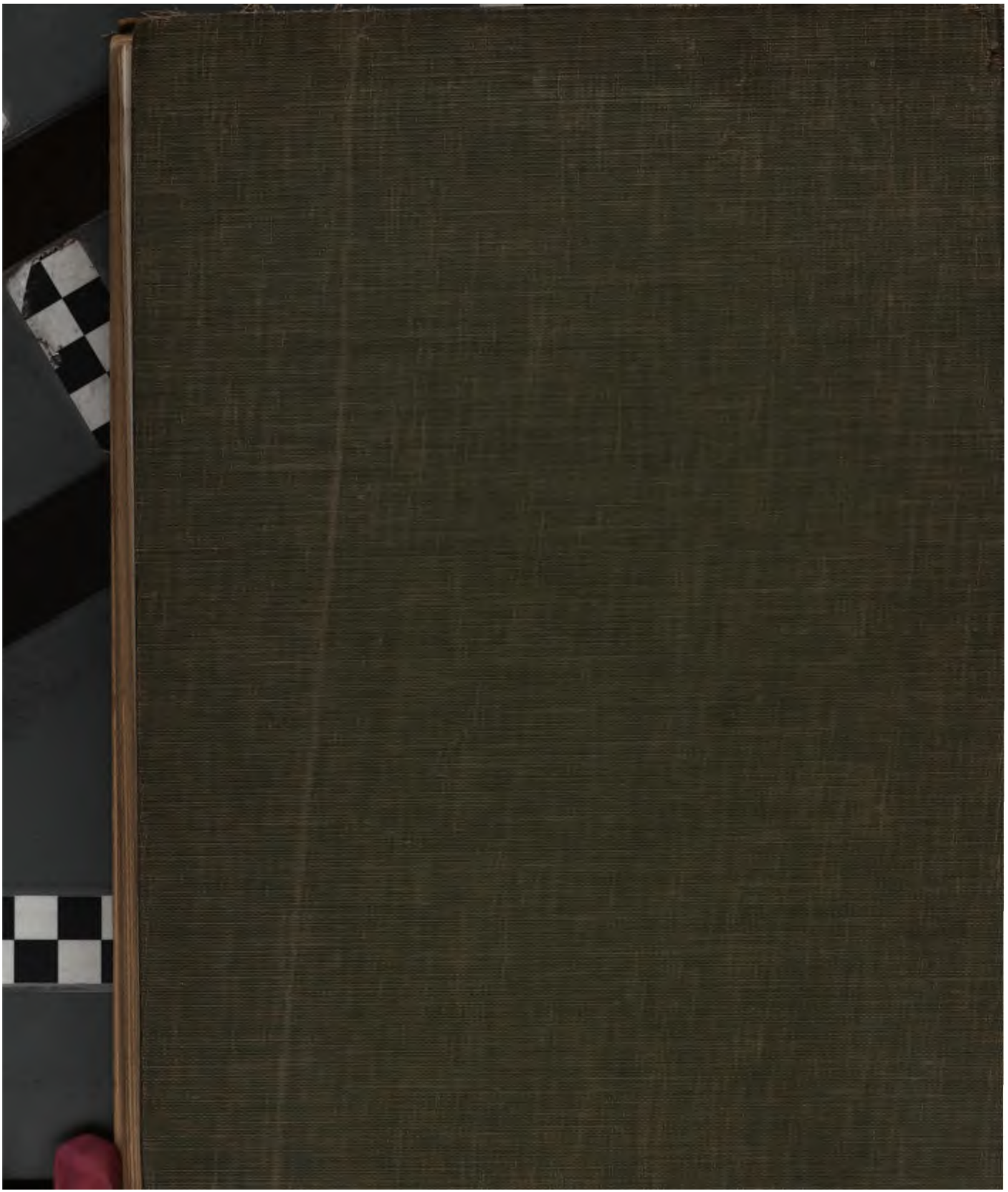
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